“ROLE OF BRONCHOSCOPY TO DETERMINE THE ETIOLOGY OF NON RESOLVING PNEUMONIA IN A TERTIARY CARE INSTITUTE”

DISSERTATION

SUBMITTED TO THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI

In partial fulfillment of
the requirements for the degree of

M.D. (TUBERCULOSIS &RESPIRATORY MEDICINE)

BRANCH – XVII

DEPARTMENT OF THORACIC MEDICINE

TIRUNELVELI MEDICAL COLLEGE HOSPITAL

TIRUNELVELI - 627011

APRIL-2017

CERTIFICATE

CERTIFICATE BY THE DEAN

I hereby certify that this dissertation entitled **"ROLE OF BRONCHOSCOPY TO DETERMINE THE ETIOLOGY OF NON RESOLVING PNEUMONIA IN A TERTIARY CARE INSTITUTE"** is a record of work done by **Dr.T.PUDHUMALAR**, in the Department of THORACIC MEDICINE , Tirunelveli Medical College, Tirunelveli, during her postgraduate degree course period from 2014- 2017. This work has not formed the basis for previous award of any degree.

The DEAN

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CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"ROLE OF BRONCHOSCOPY TO DETERMINE THE ETIOLOGY OF NON RESOLVING PNEUMONIA IN A TERTIARY CARE INSTITUTE"** , is a record of work done by **Dr.T.PUDHUMALAR,** in partial fulfillment for the award of the degree of Doctor of Medicine in THORACIC MEDICINE for the April 2017 examination by the Tamilnadu Dr.M.G.R. Medical University, Chennai , this is a bonafide original research work done by her in the department of TUBERCULOSIS AND RESPIRATORY MEDICINE , Tirunelveli Medical College, under my guidance and supervision.

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DECLARATION BY THE CANDIDATE

I solemnly declare that this dissertation titled **"ROLE OF BRONCHOSCOPY TO DETERMINE THE ETIOLOGY OF NON RESOLVING PNEUMONIA IN A TERTIARY CARE INSTITUTE"** submitted by me for the degree of M.D., is the record work carried out by me during the period of 2014-2017 under the guidance of **Prof. Dr.K.KRISHNAMOORTHY, M.D**, Professor and Head of the Department, Department of Thoracic Medicine, Tirunelveli Medical College, Tirunelveli. The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai, towards the partial fulfilment of requirements for the award of M.D.(Branch XVII) Tuberculosis and Respiratory Medicine examination to be held in April 2017.

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PROTOCOL TITLE: ROLE OF BRONCHOSCOPY TO DETERMINE THE ETIOCOGY OF NON RESOLVING PHEUMONIA IN A TERTIARY CARE INSTITUTE.

PRINCIPAL INVESTIGATOR: Dr. PUDHUMALAR, MBBS.;

DESIGNATION OF PRINCIPAL INVESTIGATOR: POST GRADUATE IN THORACIC MEDICINE
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Dear ,Dr. Pudhumalar, MBBS., The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during the IEC meeting held on 10.06.2015.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☐
7.	Curriculum Vitae of the Principal Investigator	☐
8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☐
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed.
3. A written request should be submitted 3weeks before for renewal / extension of the validity
4. An annual status report should be submitted.
5. The TIREC will monitor the study
6. At the time of PI's retirement/leaving the institute, the study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and the revised budget form should be submitted.
   c. If the amendments require a change in the consent form, the copy of revised Consent form should be submitted to Ethics Committee for approval. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented.
   d. If there are any amendments in the trial design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the IEC, only then can they be implemented.
   e. Approval for amendment changes must be obtained prior to implementation of changes.
   f. The amendment is unlikely to be approved by the IEC unless all the above information is provided.
   g. Any deviation/violation/waiver in the protocol must be informed.

STANDS APPROVED UNDER SEAL

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ABBREVIATIONS

1.	AFB	Acid fast bacilli
2.	aPTT	Activated partial thromboplastin time
3.	ATS	American Thoracic Society
4.	BTS	British thoracic society
5.	BAL	Broncho alveolar lavage
6.	CAP	Community acquired pneumonia
7.	COP	Cryptogenic organizing pneumonia
8.	COPD	Chronic obstructive Pulmonary disease
9.	CBNAAT	Catridge based nucleic acid amplification test
10.	CT	Computed tomography
11.	ELISA	Enzyme linked immunosorbent assay
12.	FOB	Fiberoptic bronchoscopy
13.	FNAC	Fine needle aspiration cytology
14.	HIV	Human immunodeficiency virus
15.	IDSA	Infectious disease society of America
16.	LRI	Lower respiratory infection
17.	LPA	Line probe assay
18.	MGIT	Microscopic growth indicator tube
19.	MTB	Mycobacterium tuberculosis
20.	NRP	Non resolving pneumonia
21.	TBLB	Transbronchial lung biopsy
22.	TBNA	Transbronchial needle aspiration
23.	PT	Partial thromboplastin time
24.	PCR	Polymerase chain reaction

CONTENTS

INTRODUCTION

Pneumonia is defined as inflammation of the pulmonary parenchyma caused by an infectious agent [1]. Inappropriate or delayed treatment leads to morbidity, mortality and drug resistance in significant number of population.

Non resolving pneumonia is one of the common clinical problem. Infection with drug resistant organisms, Misdiagnosis of pathogen, presence of co morbid conditions, development of complications, non infective etiology are some reasons for non resolution. Selection of patients and appropriate timing of further evaluation can be challenging. There is no uniform diagnostic or treatment approach for patients with non resolving pneumonia.

Along with other routine investigations, Fiberoptic bronchoscopy (FOB), Computed Tomography scan of the thorax and CT-guided fine needle aspiration cytology (FNAC) may be helpful in the evaluation of non-resolving or slowly resolving pneumonia. FOB is one of the most useful procedure in the evaluation of patients with non resolving pneumonia.

This study is to establish the etiology of non resolving pneumonia by using FOB.

REVIEW OF LITERATURE:

Pneumonia:

Pneumonia is defined as inflammation of the pulmonary parenchyma caused by an infectious agent [(1)].Pneumonitis reflects inflammation due to both infectious and non infectious cause. Various terminologies are used to describe various forms of pneumonia which reflects the possible etiology .These include aspiration pneumonia, community acquired pneumonia, nosocomial pneumonia,ventilator associated pneumonia etc.

Pneumonia is one of the leading cause for mortality and morbidity worldwide. Inappropriate or delayed treatment leads to mortality,morbidity and drug resistance in significant number of population. Community acquired pneumonia (CAP) is one of the common clinical problem characterized by cough, fever, chills, fatigue, dyspnoea, rigors, and pleuritic chest pain—with or without new infiltrate on chest radiography. Majority of patients it responds well with initial empirical antibiotics. Only few patients respond poorly, resulting in non resolving pneumonia or death. Despite advance in medical management, the mortality rate remains 5 to 15 % [(2)] Pneumococcus and multiorganism infection are the most common causes which require treatment in an intensive care unit.

ETIOLOGY:

Streptococcus pneumoniae is the most common cause of community acquired pneumonia(CAP).Hemophilus influenza and Moraxella catarrhalis, are more common in patients who have underlying chronic lung disease like COPD. Staphylococcus aureus, occurs more commonly during an influenza outbreak. Individuals on long term steroids, or alcoholics, frequent exposure to antibiotic and those with severe underlying bronchopulmonary disease are at risk of infection with Enterobacteriaceae species and P. aeruginosa. Less common causes of pneumonia include Streptococcus pyogenes, Neisseria meningitidis, Pasteurella multocida and H. influenzae.

The "atypical" organisms, which include Mycoplasma pneumoniae, Chlymadia pneumoniae, Legionella are other causes. These are more prevalent among outpatients.

Viral causes of CAP in Adults : RSV, adenovirus, and parainfluenza virus, Human meta pneumovirus, herpes simplex virus, Varicella-zoster virus, SARS-associated coronavirus, and measles virus. Viral etiology(18%) identified as a cause of community acquired pneumonia in a recent study among immunocompetent adult patients .Respiratory Syncytial Virus was the most common pathogen identified in this study . They concluded viral pneumonia also common among outpatients[(3)].

Other etiologic agents rarely idenified are:

- Chlamydia psittaci [psittacosis],Coxiella burnetti[Q fever],Francisella tularemia[tularemia],Bordetella pertussis[whooping cough].
- Fungai- Histoplasma capsulatum, Cryptococcus neoformans, Blastomyces hominis, Coccidioides immitis.

They are less common and only 2 to 3 % of total.

Anerobes -common cause of aspiration pneumonia.

Risk Factors:

Causative organisms from the upper airways or less commonly from hematogenous spread or direct spread from a contiguous focus find their way to lung parenchyma. Conditions such as altered sensorium, stroke facilitate aspiration of contents into lungs. Loss of upper airway reflexes such as cough, impairment of local defense mechanism such as mucosal blanket which is lost due smoking and irritants ,factors that destroy alveolar epithelium such as tobacco smoking, bronchial metaplasia or neoplasia, pulmonary edema and congenital causes such primary ciliary dyskinesia contribute to occurrence of pneumonia

PATHOGENESIS:

The host defense system include intact mucosal epithelium, ciliary mechanism, white blood cells, alveolar macrophages ,inflammatory mediators like interleukins, chemokines etc. Microrganisms commonly enter the respiratory tract but immune defense mechanisms, help in clearing

them. Pneumonia occurs when there is impaired host defense ,or as a result of infection with virulent organisms, a large “dose” of bacteria. Microbes gain access to the lung by any of the following routes:

- Micro aspiration from the upper respiratory tract
- Droplet infection from infected person
- Spread from contiguous infected sites
- Hematogenous spread

Once the pathogen or agent enters the bronchi and bronchioles, it firmly fixes with the wall and causes cascade of inflammation in the host body. There are two main types of acute pneumonia : bronchopneumonia (with lobular topography) and lobar pneumonia (lobar topography). Lobar pneumonia causes exudative inflammation of an entire pulmonary lobe. If not treated, lobar pneumonia evolves in four stages.

1.exudative phase2.red hepatizaton3.gray hepatization 4.resolution

Common to all stages is the enlargement of the affected lobe with loss of its spongy appearance.

EVALUATION OF PATIENTS WITH SUSPECTED PNEUMONIA:

a)Detailed clinical history which includes age, onset of symptoms, resident area, recent travel, prior hospital admission, antimicrobial treatment, co morbid conditions can give some clue to etiology.

b)General examination and respiratory system examination is vital.Physical examination may not be reliable in immuno compromised individual.

c)Investigations:

- complete blood count,C reactive protein,Blood culture:polymorpho leucocytosis is observed in bacterial etiology.
- Chest X ray:Pneumonia may present with various radiological patterns which includes consolidation, bronchopneumonia, miliary pattern, nodules, abscess, effusion, interstitial pattern, lymph adenopathy
- Noninvasive microbiological testing which includes sputum examination for cytology, Gram stain, KOH mount, Ziehl Neelson or flurochrome stain,various special stain to the specific organisms,sputum for culture and sensitivity are used.
- Bacterial and viral antigen detection by using ELISA ,latex particle agglutination, PCR . For example, studies show Steptococcus pneumonia is better identified by molecular and urinary test rather than sputum culture examination.

To identify M.TB CBNAAT,LPA,MGIT like rapid diagnostic methods can be used. In patients who show poor response to treatment, additional investigations including invasive procedures are necessary to identify the cause. These include trans tracheal aspiration, FOB guided biopsy/BAL/TBNA open lung biopsy etc.

TREATMENT:

According to 2007 IDSA guidelines, initial treatment for most of the patients remains empirical.Selection of antibiotics is based on likely pathogen and knowledge of local susceptibility patterns. We should consider individual risk factor for each of the patients and must treat accordingly.

For sick patients admitted, the first antibiotic dose should be administered as early as possible. Patients with CAP should be treated for a minimum of 5 days , should be afebrile for 48–72 h, and should have no more than 1 CAP-associated sign of clinical instability before discontinuation of therapy.A longer duration of therapy may be needed if initial therapy was not active against the identified pathogen or if it was complicated by extrapulmonary infection.

- Out patients with no risk factors a macrolide or doxycyline is recommended.
- Outpatients with co morbidities such as heart, lung, liver

or renal disease; diabetes mellitus; alcoholism; malignancies;asplenia; immunosuppressing conditions or use of immunosuppressing drugs, a respiratory fluoroquinolone or combination of Beta lactam antibiotic with macrolide is recommended.

- In areas with a high rate of infection with high-level (MIC _16 mg/mL) macrolide-resistant Streptococcus pneumoniae use of alternative drugs is recommended.
- Hospitalised patients who are stable can be treated with either respiratory fluoroquinolones or combination of β- lactam with macrolides.

  Inpatients requiring intensive care: β-lactam with azithromycin **or** a respiratory fluoroquinolone (strong recommendation) (for penicillin-allergic patients, a respiratory fluoroquinolone and aztreonam are recommended)

Special concerns:

If *Pseudomonas* infection is suspected, An antipseudomonal β-lactam (Piperacillin tazobactam,cefepime, imipenem, or meropenem) plus either ciprofloxacin or levofloxacin should be used.Other options are anti Pseudomonal β-lactam plus an aminoglycoside and azithromycin Or The above b-lactam plus an aminoglycoside and an antipneumococcal fluoroquinolone (for penicillin-allergic patients, substitute aztreonam for above b-lactam)

If MRSA is a consideration, vancomycin or linezolid should be added.

NON RESOLVING PNEUMONIA:

Non resolving pneumonia is one of the common clinical problems encountered. The problems may range from simple delay in recovery to life-threatening progressive pneumonia.

Definition of non resolving pneumonia :

Defining non resolving pneumonia is difficult, because of lack of a clear cut and validated definition in the literature. In 1943, the term unresolved organizing or protracted pneumonia was first described by Amberson[5].

Non resolving pneumonia is a clinical syndrome in which focal infiltrates begin with some clinical association of acute inflammation and despite minimum of 10 days antibiotics patient either don't improve or worsen or radiographic opacities fail to resolve within 12 weeks[6] .

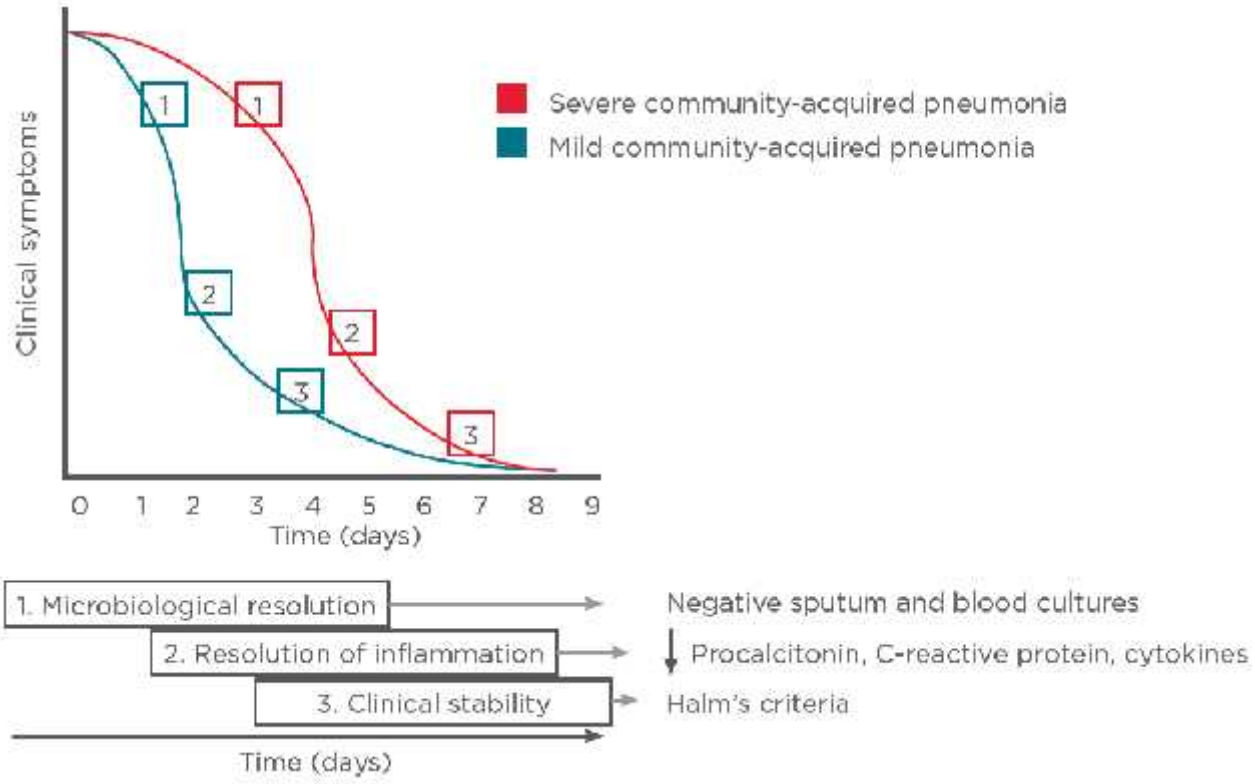
According to IDSA/ATS 2007 guidelines, non resolving or slow-resolving pneumonia refers to patients who present with persistence of pulmonary infiltrates more than 30 days duration after initial pneumonia-like syndrome.

Kirtland and Winterbauer defined non resolving pneumonia is less than complete clearance of radiological infiltrates in 4 weeks or less than 50% clearance in chest infiltrates in patients who defervesed and improved

symptomatically or non resolution of radiological infiltrates in an expected period of time based on initial diagnosis and at least 10 days of antibiotics[7].

NORMAL VERSUS DELAYED RESOLUTION:

Resolution of pneumonia is not defined easily and it depends upon the underlying etiology. Clinical recovery of the patients occur earlier when compared to radiological resolution. Radiological resolution can take up to six weeks. Microbiological resolution occurs with appropriate treatment. After treatment, inflammation of lung parenchyma decreases and patients improve clinically[8,9].



Fig(1): Course of recovery in community acquired pneumonia

Empirical treatment is mainstay of treatment in CAP but studies show 6 to 15 % of inpatients are not cured by initial treatment[10,11].At the same time, treatment failures among outpatients unit is so far not well studied. The overall mortality was around 49% in hospitalised patients with severe CAP who were not responding to the treatment[11] . In another study the mortality rate was 27% [10].

According to the IDSA 2007 guidelines, treatment failure in CAP is classified systematically in the following ways. The first entity is progressive pneumonia or actual clinical deterioration, with acute respiratory failure requiring ventilatory support and/or septic shock, usually occurring within the first three days of hospital admission. The second pattern is that of persistent pneumonia which was defined as absence of or delay in achieving clinical stability, using the Halm's criteria.. The Infectious Diseases Society of America/ American Thoracic Society (IDSA/ATS) 2007 guidelines recommend the use of Halm's criteria to define clinical stability. These clinical criteria are reliable.They are applicable in various healthcare systems .

Halm's criteria consist of seven variables: 1.Temperature ≤37.8 °C, 2.Heart rate ≤100 beats/minute, 3.Respiratory rate ≤24 breaths/minute, 4.Systolic blood pressure ≥90 mmHg, 5.SPO2 ≥90%, or pao2 ≥60 mmHg

6.normal mental status 7. normal oral intake[12]. 2001 ATS guidelines mentioned clinical stability, which consists of only four criteria.

1. Improvement in symptoms(cough and dyspnoea),2. afebrile (temperature <37.8 °C) for more than 8 hours, 3.normalisation of white blood cell count by 10% from the previous day 4.adequate oral intake. Minimum duration to achieve this criteria is 3 days.but in 1/4 th of patients required more than 6 days.

The final entity is non resolving or slow-resolving pneumonia used to describe patients with persistence of pulmonary infiltrates more than 30 days duration after initial pneumonia-like syndrome[13]. Around 20% of these patients have diseases other than CAP when carefully evaluated[14].

Most of the time, normal resolution of pneumonia mainly correlates with radiological resolution. Persistance of radiological abnormalities with improvement in clinical status is defined as slow resolution[15] .

Complete radioglogical clearing occurs by one to three months in nonbacteremic cases and three to five months in bacteremic cases. Residual radiographic abnormalities are rare in nonbacteremic cases but are present in up to 35 percent of bacteremic cases[16].

Using systematic approach, which include routine investigations with appropriate invasive procedures, , specific etiology was acheived in 73% cases ,in a series of patients with non resolving pneumonia [17] .

Factors affecting resolution of pneumonia are:

a) development of complications

b) infection with drug resistant organisms

c) misdiagnosis of pathogen

d) presence of comorbid conditions

e) non infective etiology

a) Complications:

Infectious complications which include empyema, complicated parapneumonic effusion, and lung abscess. Sequestered foci of infection can prevent adequate concentrations of antibiotics to reach the particular site and prevent resolution

b) Virulence and drug resistance:

Streptococcus pneumoniae is the most common cause of community acquired pneumonia and also responsible for majority of non resolving pneumonia especially in patients with comorbidities.In pneumococcal pneumonia, clinical symptoms subsided in majority of patients within 2 to 3 days of appropriate treatment. Around 6 % of patients remain febrile beyond 20 days[18]. In around 20 to 30 % of patients the radiological resolution was slower. In case of legionella infection initial worsening of radiological

changes followed by slow resolution begin only after 2 to 3 weeks. Around 50 % of infected patients will show radiological resolution by 10 weeks. Residual fibrosis was noted in one fourth of patients. In case of Mycoplasma pneumoniae rapid resolution is a rule.40% of patients will show complete resolution at 4 weeks and 90% of patients at 8 weeks.

Like Mycoplasma,Chlamydia pneumonia infection is moreover milder form of disease.50% of radiological changes resolve within 4 weeks.In 20% of patients it may take 9weeks.Residual abnormalities are seen in 20 to 30%..After the introduction of conjugate vaccine, the incidence of Hemophilus infection has drastically reduced in children worldwide.In adults the course of Hemophilus disease not well studied. Available reports show slow resolution and prolonged hospitalization in adults with Hemophilus influenza pneumonia.

Apart from this ,resistant organisms like MRSA,MDR TB, multidrug resistant gram negative bacilli, pencillinase resistant Streptococcus pneumonia are responsible for delay in resolution.

c) Misdiagnosis of organism:

Tuberculosis is one of the most common etiology for non resolving pneumonia. In atypical presentation, sputum examination is often less reliable and need more invasive procedure to detect Mycobacterium. Fungal

infections like Histoplasmosis, Coccidioidomycosis, Blastomycosis, Mucormycosis, Cryptococcus,

Aspergillus infection and Nocardia, Actinomycosis like organisms are also responsible for non resolving pneumonia. Studies show Aspergillus may mimic as bacterial pneumonia and are treated with multiple antibiotics before the diagnosis is established[19].

d) Comorbid factors:

Associated co morbid conditions delay the resolution of pneumonia. Only 20 o 30 % of patients with comorbid conditions will show radiological resolution by 4 weeks[20]. Extremes of age will show delay in resolution. 30% of patients who were older than 50 years will show slower radiological resolution.

e) Non infective cause:

Noninfectious causes are responsible for non resolution of pneumonia in 20 % of patients . In a study performed by Arancibia et al, in patients hospitalised for CAP, 19 patients had progressive pneumonia and 30 had non resolving pneumonia. Out of this, around 65% cases were due to infections . Persistance of primary infection was noted in 23 patients, 11 had developed a nosocomial infection, and non-infectious disorders like

neoplasm, foreign body, interstitial lung disease were present in 9 patients[17].

i) Neoplasms :

Primary Lung cancer or metastasis are responsible for non resolving pneumonia .The possible mechanisms are endobronchial obstruction or extrinsic compession which mimic pneumonia, secondary postobstructive pneumonia or abscess, or by mimicking an infiltrative process. Bronchogenic carcinoma and carcinoid tumors are the most common cause of endobronchial obstruction leading to pneumonia. Bronchoalveolar cell carcinoma and lymphoma are the most common causes of an alveolar infiltrate mimicking pneumonia. The frequency of endobronchial carcinoma as a cause of nonresolving pneumonia is Low, ranging from 0 to 8 percent in most series[21].Bronchoscopy, CT guided biopsy etc. are needed to diagnose malignancy.

ii) Inflammatory disorders

Cryptogenic organising pneumonia, diffuse alveolar damage, alveolar haemorrhage, eosinophilic pneumonia, hypersensitivity pneumonitis, vasculitis lipoid pneumonitis, pulmonary alveolar proteinosis, acute interstitial pneumonia ,connective disease disorders may mimic pneumonia

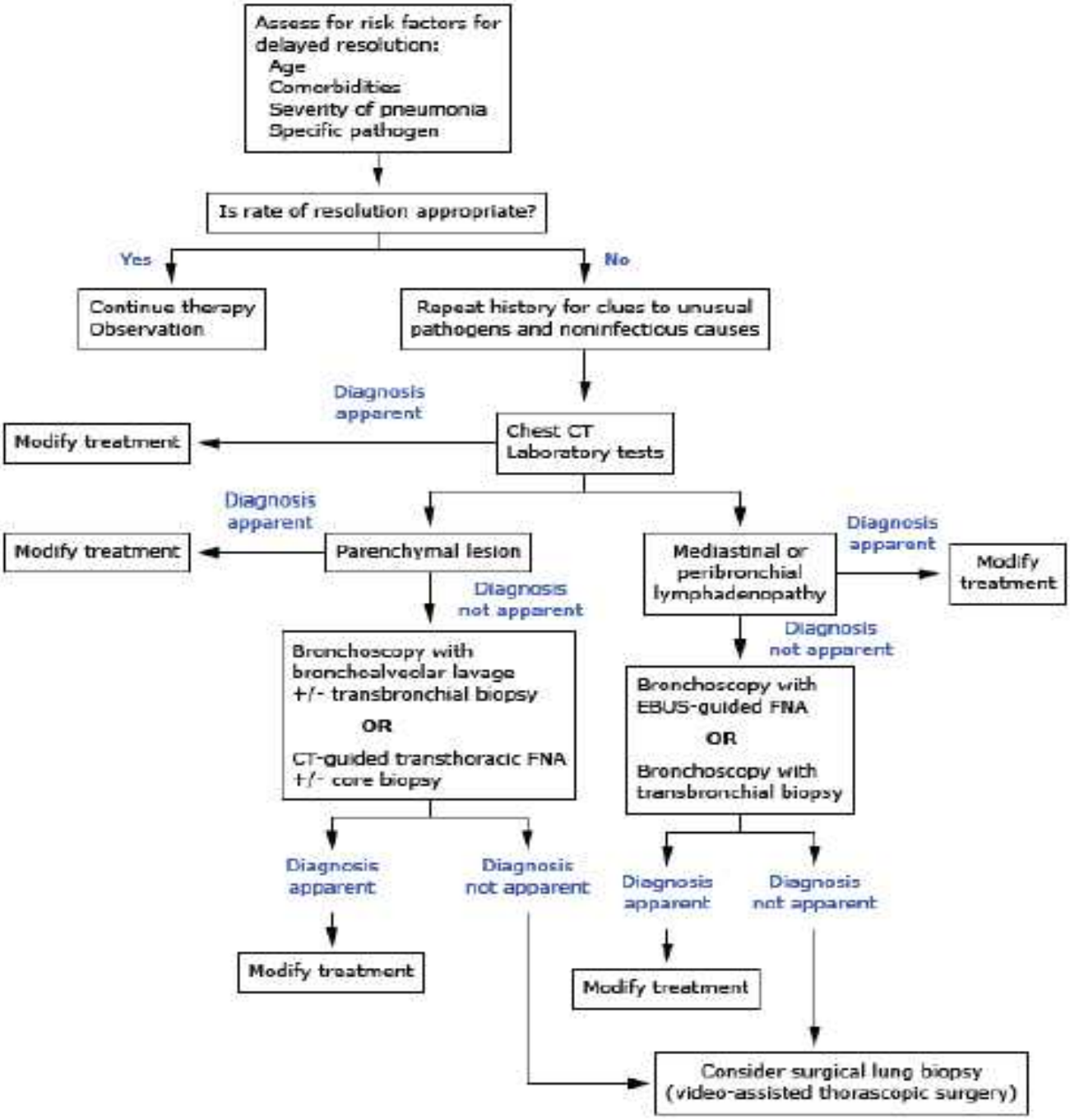
.

iii) Drugs

Drug induced lung disease can be confused with infectious pneumonia. Examples include Amiodarone, Bleomycin, Methotrexate, Nitrofurantoin. Amiodarone toxicity is an important mimic of NRP and can present as focal alveolar infiltrates.

There is no clear guidelines regarding appropriate antimicrobial therapy for non responding pneumonia . Majority of cases of non resolution are due to the severity of disease at presentation, associated co morbid factors. For severe pneumococcal pneumonia, combination therapy was found to be useful[22]. In case of NRP, rather than using multiple broad spectrum antibiotic course, other etiologies should be considered and proceeded with necessary investigations This will help the patients to get appropriate treatment in appropriate time which in turn will reduce morbidity and mortality.

Fig:2 APPROACH TO NON RESOLVING PNEUMONIA



BRONCHOSCOPY

The ease and safe access to visualise bronchial tree has been a long standing desire . After various evolution, today's flexible bronchoscope utilises modern technology for better differentiation and contrast enhancement.

Bronchoscopy is a valuable diagnostic and therapeutic tool in Pulmonary Medicine. It plays an important role in the diagnosis of non resolving pneumonia.

HISTORY:

Gustavkillian is considered as the father of modern bronchoscopy. Chevalier Jackson developed a rigid esophagoscope . Derivatives of this device are now called rigid bronchoscopes. Shigeto Ikeda , a thoracic surgeon, developed flexible fiberoptic bronchoscope in the year 1968, which is now known as the year of "second revolution" in bronchoscopy[23] Andersen was the first to perform bronchoscopic transbronchial lung biopsy (TBLB) via the rigid bronchoscope in 1965. In 1958, Eduardo Schieppati originally proposed transbronchial needle aspiration biopsy (TBNA) [24]. Inspired by the initial experiences of Oho and his colleagues[16] , Ko-Pen Wang (1978) published the first report on the successful bronchoscopic needle aspiration biopsy of paratracheal tumors through a flexible bronchoscope.

BRIEF REVIEW OF FLEXIBLE BRONCHOSCOPY DESIGN

The parts of FOB are eye piece, suction valve, angulation knob, working channel, insertion tube, light guide connector (fig:3.)

Fig 3:Parts of Flexible Bronchoscopy.

Bronchoscope is designed in such a way to accommodate adequate number of glass fibres. This helps in transmitting light into the lumen and transport image from the distal end of the scope to the eyepiece.

The proximal tip of the bronchoscope can be angulated by a lever which is located at the control section (the central part of the scope). The

bronchoscope can be bent only in two directions 180°and 130°. The imaging fibre bundle in flexible fibreoptic bronchoscope is an important component which determines the quality of image. Clearer the image, better is the chance of diagnosis so that therapeutic options can be planned accordingly. Each single fibre has the same dimension which is accurate .It is positioned at similar position at both ends of the fibre bundle. If this is not achieved, artefacts impair the the quality of image.(Figure 4)

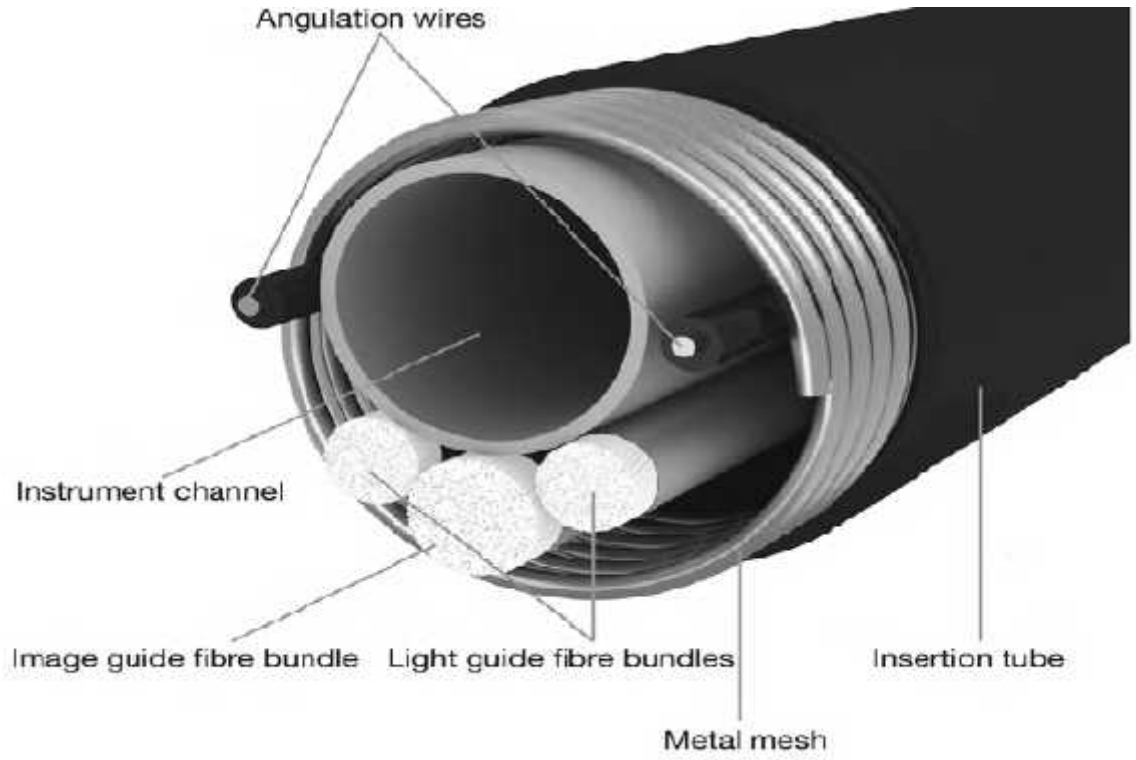


Fig 4 :various internal parts of FOB

There are various channel ports in the bronchoscope.

a) The suction valve in control section is used for aspiration of mucus. It is connected to an external suction apparatus . Using this valve, suction can be done by the physician .

b) The working channel or instrument channel port is located bit deep at the lower part of the control section.(Figure 3). Endotherapy instruments can be inserted into the bronchoscope using this port to reach the site of interest.. e.g. to guide biopsy forceps and to take sample for further investigation. It is also called biopsy channel. In order to save space, the instrument channel is positioned to join the suction channel at the lower part of the control section.

TABLE 1: SPECIFICATIONS OF FLEXIBLE BRONCHOSCOPE

Outer diameter	<6 mm
Imaging fibre bundle	
Single fibre diameter	<15 μm
Number of fibres	>15,000
Focus	5–30 mm
Angulation of distal end	60 ° at 30 mm from distal end
Length of the rigid part of distal end	<10 mm
Total length	~1 m
Field of view	80 °, prograde

Endobronchial ultrasound (EBUS) , Navigation bronchoscopy (NB), Ultrathin bronchoscopes(To visualise 6^{th} to 8^{th} generation bronchi in adults and helps to detect more peripheral lesions[26]), Autofluorescence bronchoscopy (To detect central intraepithelial moderate or severe dysplasia) are advanced technique used nowadays for diagnostic purpose.

Bronchoscopy can be used both for diagnostic and therapeutic purposes.

Diagnostic Uses: Following procedures used to obtain diagnostic material.

1.Bronchoalveolar lavage(BAL)

2.Bronchial wash

3.Brushing

4.Transbronchial or (TBLB)

5.Endobronchial lung biopsy. (EBB)

6.Transbronchial needle aspiration.(TBNA)

Therapeutic Uses: Following therapeutic procedures can be done.

- Balloon dilatation
- Argon plasma coagulation
- Laser Electrocautery
- Brachytherapy etc.

British Thoracic society (2001) recommends the following guidelines for bronchoscopy.

BEFORE BRONCHOSCOPY:

- Verbal and informed consent should be obtained before the procedure
- Solid diet can be allowed upto 4 hours prior to procedure
- Liquid intake upto 2 hours before procedure
- Prophylactic antibiotics should be given before bronchoscopy to patients with asplenia, prosthetic heartvalve, or previous history of endocarditis.
- FOB should be avoided for atleast 6 weeks following myocardial infarction.
- Atropine is not required routinely prior to the procedure.
- Oral anticoagulants should be stopped at least 3 days before. Or their effect be reversed with vitamin K injection.

DURING BRONCHOSCOPY:

- During procedure, patients vitals should be monitored using pulse oximetry.
- SpO_2 should be maintained atleast 90% . Supplemental oxygen should be administered if necessary.
- The maximal total dose of lignocaine for topical anaesthesia should be limited to 8.2 mg/kg in adults (approximately 29 ml of a 2% solution for a 70 kg patient). In old age patients or those with liver or cardiac diseases, lesser dose should be used.
- Lignocaine gel(2%) is better compared to spray for nasal anaesthesia.

- Equipments necessary for emergency resuscitation should be kept ready.

AFTER BRONCHOSCOPY:

- Oxygen supplementation may be required in patients, particularly those with impaired lung function and those who have been sedated.
- A chest radiograph should be taken at least one hour after transbronchial biopsy to exclude air leak.

CLEANING AND DISINFECTION:

- Immersion time of 20 minutes is recommended for bronchoscopes at the beginning and end of a session and between patients.
- Longer immersion time of 60 minutes is recommended in known or suspected atypical mycobacterial infections and in HIV positive individuals with respiratory system complaints. Mycobacterium avium intracellulare and other atypical mycobacteria are more resistant to glutaraldehyde. Patients with suspected tuberculosis should undergo bronchoscopy at the end of the list.

PROCEDURE:

Figure 5 shows, step by step procedure of bronchoscopy. Gross examination of upper respiratory tract, vocal cord movements, tracheobrnchial tree followed by various procedures can be done.

MONITORING:

Patient should monitored for any fall in saturation and hemodynamic instability. vitals which includes heart rate, oxygen saturation(>92%) ,blood pressure, ecg monitoring are monitored throughout the procedure. Intravenous access necesssary for all the patients. resuscitation equipments and supplemental oxygen should be available.

All FOB procedures are performed using standard guidelines.

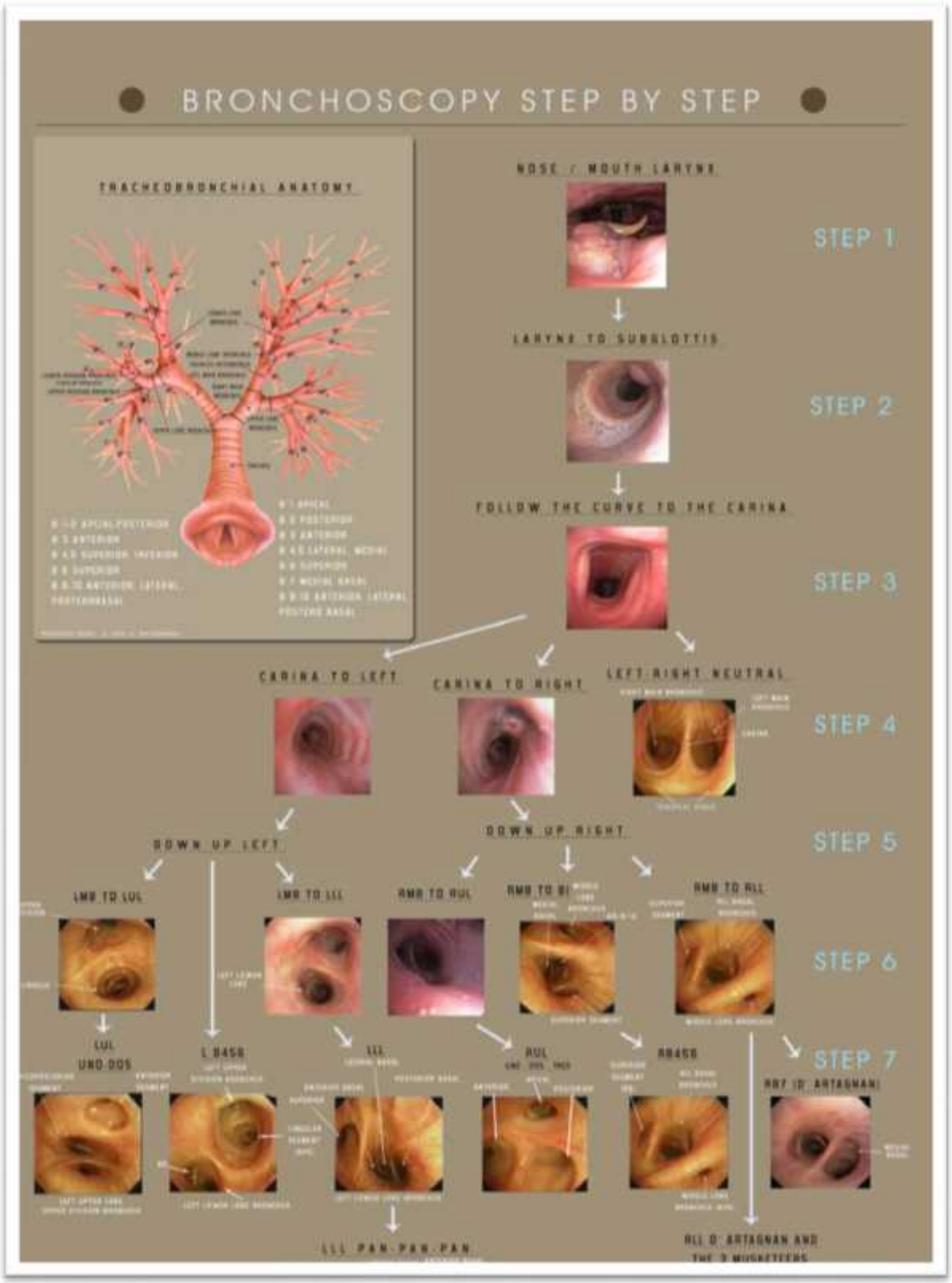


Fig 5:Bronchoscopy-step by step Approach.

Gross examination of respiratory tract during the procedure can give valuable information. Endobronchial tuberculosis, mass or mucus plug occluding the lumen are some of the causes of non resolving pneumonia which can be diagnosed by gross examination of tracheobronchial tree.

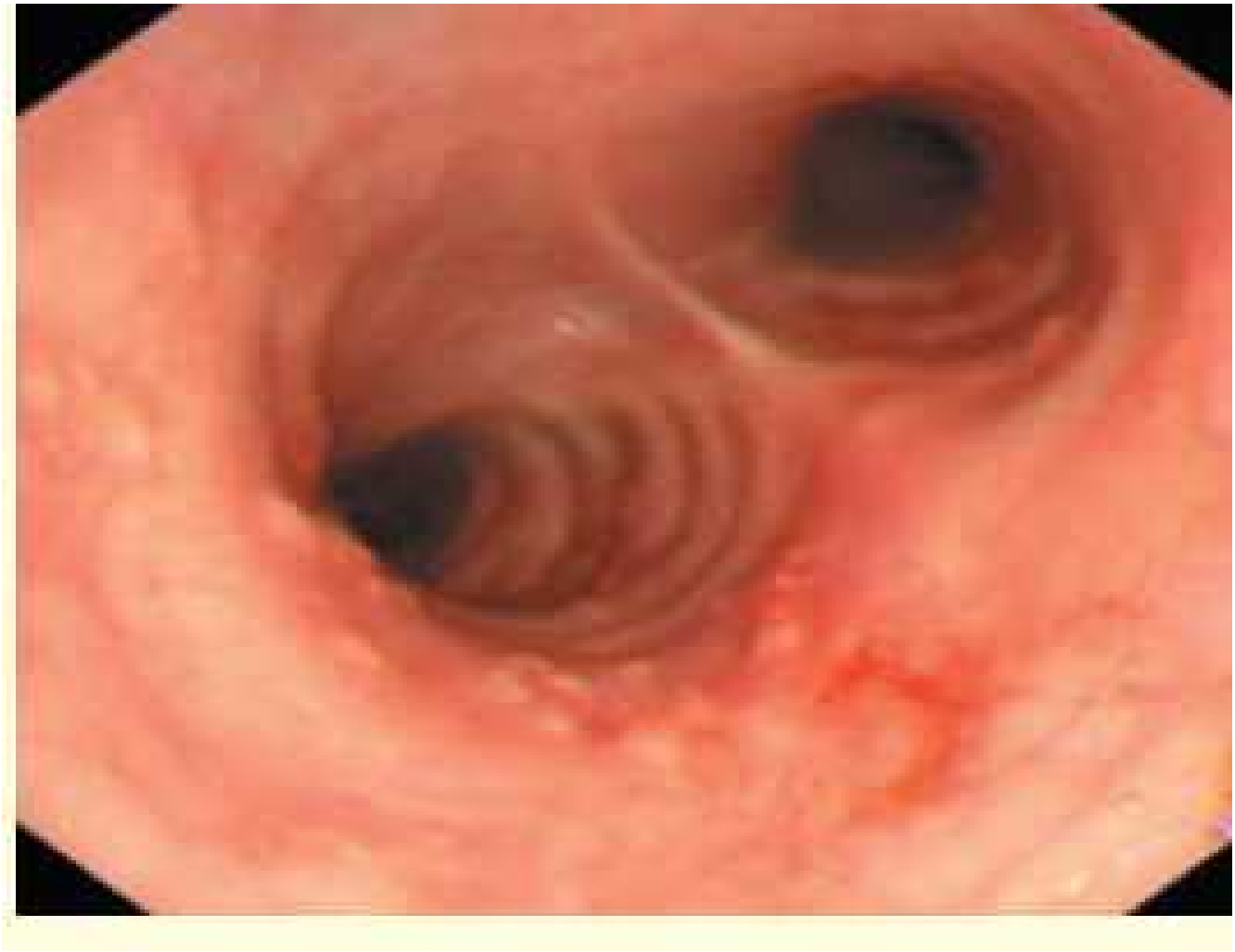


Fig 6:Nodular lesion in lower trachea due to Endobronchial TB

Fig 7:Tuberculous Granuloma occluding the anterior segment of Right Upper Lobe.

Fig 8:Mucus plugging due to allergic Bronchopulmonary Aspergilosis.

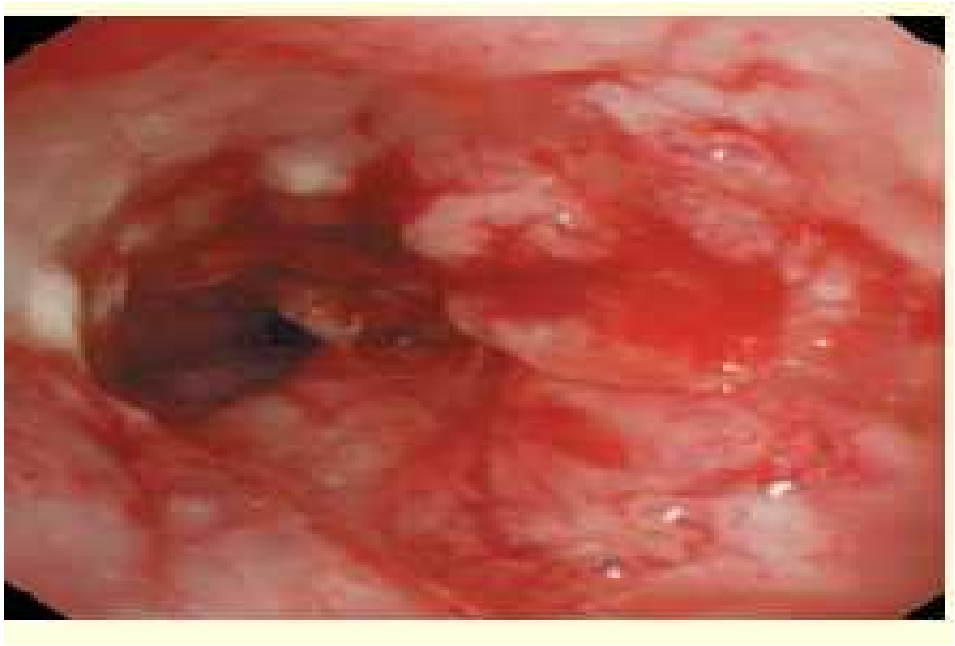


Fig 9:Irregular,narrowed lumen due to infiltrative malignant lesion occluding right main bronchus.

Fig 10:Mass lesion totally occluding the left upper lobe bronchus.

BRONCHO ALVEOLAR LAVAGE:

Bronchoalveolar lavage(BAL) is a minimally invasive important diagnostic tool in pulmonary medicine[27,28]. It is particularly useful in patients with diffuse lung abnormalities. It is also called liquid lung biopsy.

BAL fluid contains both cellular and noncellular components of the alveoli and epithelial surface of the lower respiratory tract. Components of the BAL fluid represent the inflammatory and immune status of the lower respiratory tract and the alveoli[29]. BAL procedure is a better option when compared to TBLB &TBNA in patients who are at risk of bleeding

TECHNIQUE:

Bronchoalveolar lavage is performed following general inspection of the tracheobronchial tree and before biopsy or brushing[30]. Middle lobe or lingula is the preferred site for lavage in diffuse lung disease. In focal lesions, the site with maximum radiographic changes is chosen.We should avoid suction prior to the procedure. If suction is done before the procedure, the suction channel should be cleaned thoroughly with saline.To avoid the bacteriostatic effect of local anesthesia,we should limit the use of lignocaine as much as posssible.

Bronchoscope is advanced until it reaches the wedge position .Good wedge position means that the bronchoscope is advanced as far as possible

without losing the view of lumen. Over wedging the scope will cause trauma to patient and diminish fluid recovery. Poor wedge position leads to fluid leakage around the scope and will stimulate cough soon after instillation.

20 ml of sterile normal saline is used at room temperature or warmed to 37·c to decrease the cough and increase the cellular yield. Bubbling of fluid via FOB indicates return of fluid from alveolar space. Gentle suction is used within the range of 50 to 80 mm of Hg. We have to repeat the procedure 5 to 6 times with maximum amount of fluid 100 to 120 ml. According to ATS guidelines,40 to 70 % of instilled fluid should be aspirated and sent immediately to analysis. The patient should be observed for at least 1 hour for any immediate complications following procedure. Protected broncho alveolar lavage is another method to collect uncontaminated specimen from lower airways.

Mini broncho alveolar lavage is another method which is used mainly in ICU setup to avoid more invasive procedure in patients who are already in respiratory compromise. It is performed blindly,without visualising tracheobronchial tree.Small volume of sterile saline is injected, which is then aspirated and sent for analysis. It is mainly useful to detect etiology of pneumonia in patients undergoing mechanical ventilation[31,32].

BAL fluid sent is immediately for various analysis.

- cytology and cell count
- bacterial & fungal culture and sensitivity
- BAL fluid for AFB stain and CBNAAT

Normal BAL

The BAL fluid obtained from healthy, nonsmoking adults without underlying lung disease is dominated by alveolar macrophages (>80%).

Normal content of BAL:

- Alveolar macrophages -80–90%
- Lymphocytes- 5–15%
- Polymorphonuclear neutrophils 1–3%
- Eosinophils-1%
- Mast cells-<1%

BAL Cytology:

The fluid is centrifuged and the concentrate is used to make smears, thin layer preparations, or cell blocks. Cytology of BAL is useful in identifying various type of malignancies, diffuse alveolar hemorrhage, eosinophilic lung diseases and various forms of interstitial lung diseases .

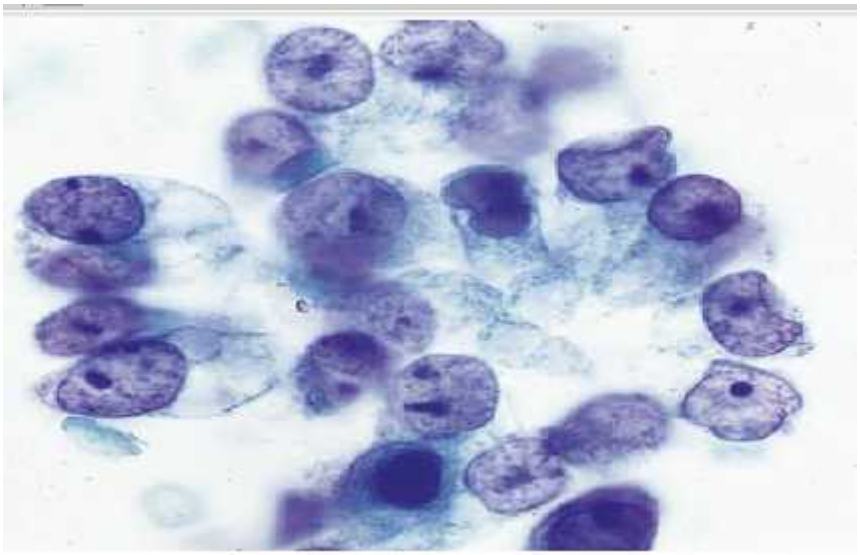


Fig 11 : BAL fluid cytology showing Adenocarcinoma. It has columnar cells with polarized nuclei and single prominent nucleoli

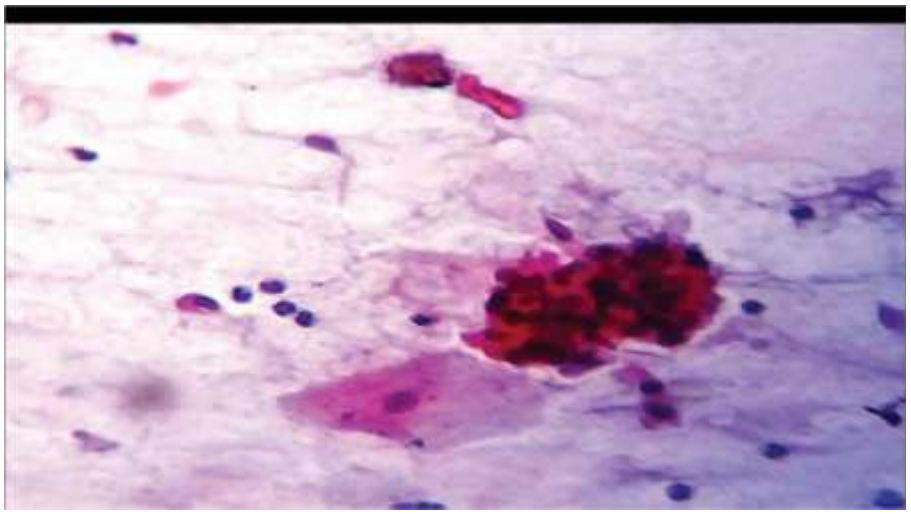


Fig 12 : BAL cytology smear: squamous cell carcinoma. Picture shows clusters of polygonal cells with eosinophilic cytoplasm and hyper chromatic nuclei.

By identifying the organisms in the BAL specimen by various staining and culture methods we can diagnose Pneumocystis jiroveci,Toxoplasma gondi,Strongyloides stercoralis,Cryptocoocus neoformans,Histoplama capsulatum, Legionella pneumoniae, Infuenza virus(A & B),Respiratory syncitial virus.

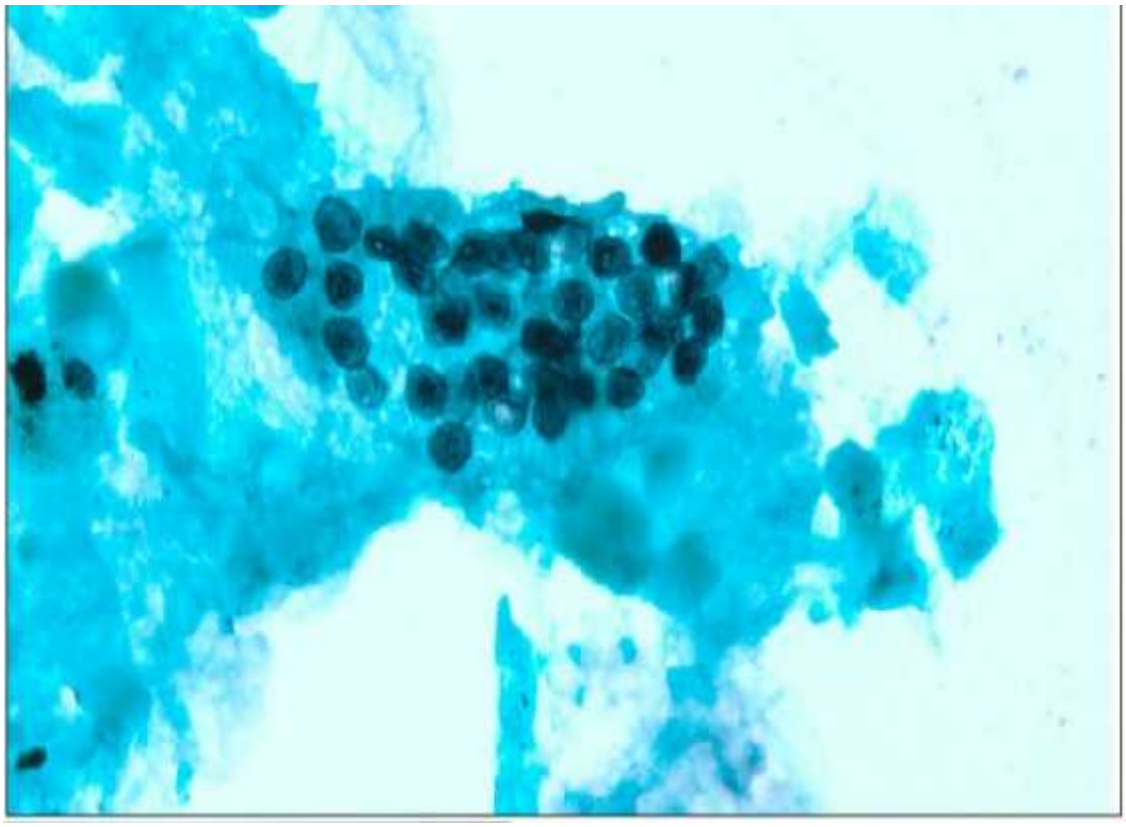


Fig 13: BAL fluid GMS(gomori methenamine silver) stain showing round to cup shaped pneumocystis.

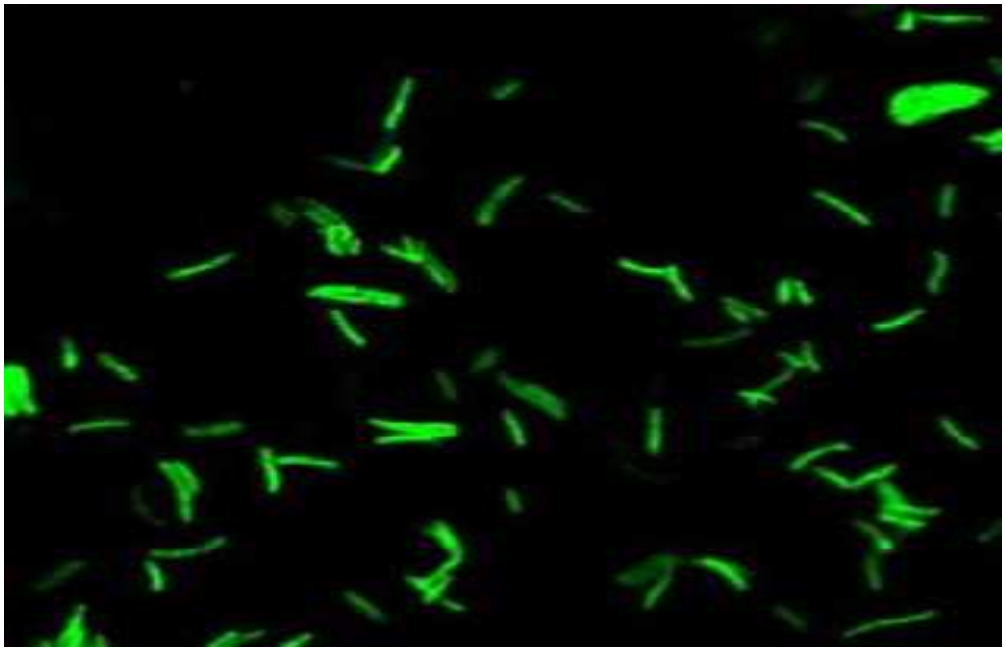


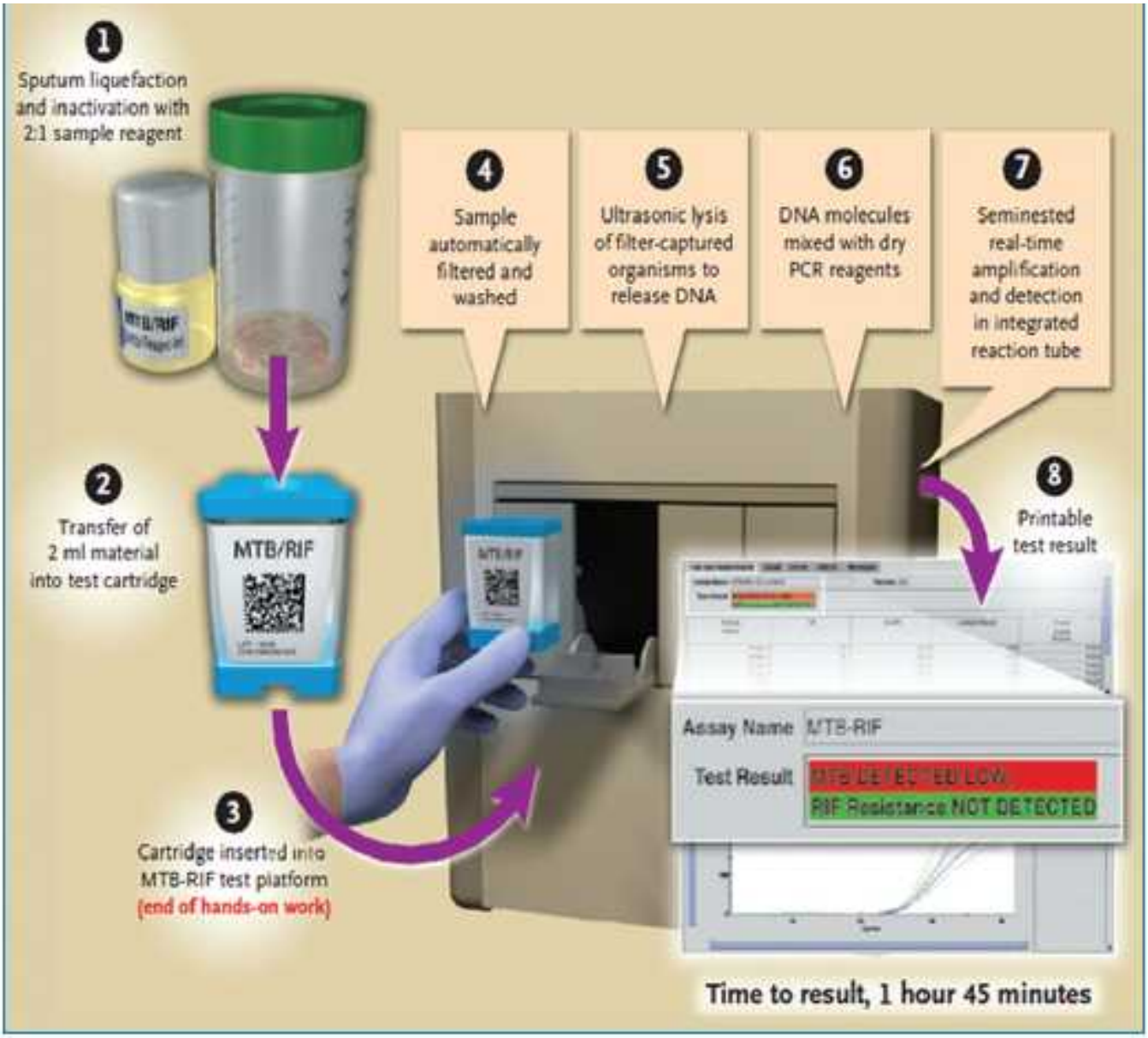
Fig 14: BAL specimen showing AFB in fluorescence staining.(0.1% Auramine stain)

DETECTION OF MYCOBACTERIUM TUBERCULOSIS:

BAL fluid subjected to fluorescence staining with 0.1% Auramine solution can detect Mycobacterium tuberculosis. Recently, rapid diagnostic method like gene Xpert/CBNAAT is used.

Nucleic acid amplification (NAA) test uses a disposable cartridge with the Gene Xpert Instrument System . Mycobacterium tuberculosis complex (MTBC) and Rifampicin resistance (RNA polymerase beta gene(rpoB) can be detected in less than 2 hours. Bronchial wash around 2-5ml and Bronchial alveolar lavage (BAL) (minimum volume of 20 50 ml) should be sent for gene xpert to detect M.TB .

Fig 15:Various steps of gene Xpert plotted in the following diagram.



BAL analysis is a useful diagnostic tool in nonresolving pneumonia. Quantitative analysis of BAL which show more than 10^4 CFU/ml is useful to diagnose pneumonia .Sensitivity was around 22 to 93% and the specificity was 45 to 100% depending upon the clinical condition of the patients. A

study by Van der Eerden and colleagues revealed FOB was additional diagnostic value in in 49% of patients who were unable to raise sputum for Gram stain and culture and in 52% of patients for whom treatment failed[33].BAL fluid taken after starting antibiotic treatment may significantly reduce the yield , but Feinsilver et al reported, 86% yield in patients with nonresolving pneumonia who were already treated with antibiotics[29].

In immunocompromised individuals the yield is higher, around 93%.The results of BAL have been shown to change disease management in up to 84% of immunocompromised cases[35]. The diagnostic yield of BAL for peripheral cancerous lesions range from 4 to 68%[36].

According to ATS guidelines, following BAL no complications were identified in upto 95% of patients.Transient fever was noticed in 2.5% of patients.Transient pulmonary infiltrates are also described ,but usually subside within 24 hours. Their incidence increases with total amount of fluid and number of segments lavaged. Persistant fever and progressively increasing pulmonary infiltrate indicate postbronchoscopic pneumonia warranting the need for antibiotic therapy[37].Transient bronchospasm(<1%),transient hypoxia,transient fall in pulmonary function tests are other complications.

BRONCHIAL WASHINGS:

Bronchial washings is an easy procedure useful to diagnose mainly airway diseases.

Procedure:

10 to 20 ml of sterile saline is instilled into the airways and then aspirated immediately.The aspirated material is then subjected for analysis. The diagnostic yield of bronchial washings in various studies vary from 27 to 90% .The yield is highest for central lesions.

TRANSBRONCHIAL LUNG BIOPSY:

Biopsy of the lung was performed by open surgical methods until 1963, when Dr. Anderson performed bronchoscopic lung biopsy with a rigid bronchoscope.

In 1974, Levin et al, published their experience with transbronchial biopsy using flexible bronchoscopy. Various lung pathologies can be diagnosed using transbronchial lung biopsy. It is mostly performed with topical anaesthesia. This procedure not required hospitalisation . Transbronchial biopsy is employed in the setting of neoplastic disease, interstitial lung disease, pulmonary infection, unusual and unclear lung disease, and lung transplantation.

BEFORE PROCEDURE:

A detailed history, physical examination, Chest X-Ray, CT chest, informed consent are essential before procedure. Lab tests include

- Prothrombin time (PT-INR)
- Activated partial thromboplastin time (aPTT)
- Renal functions tests-serum urea, creatinine
- Liver function tests are necessary in special situations like patient on anticoagulants, uremic patients.

TBLB can be done only when:

- PT-INR less than 1.5
- aPTT less than 50 seconds.
- Platelet counts more than 50,000 .
- Clopidogrel, should be stopped one week before procedure. Warfarin should be withold 3 days before procedure. Unfractionated heparin should be stopped before six hours . But aPTT should be monitored before the procedure. For patients using low moleular weight heparin(LMWH),with hold at least 12 hours before the procedure. Patients using Aspirin or NSAIDS can be allowed to continue their medication.

Procedure:

After the gross examination of tracheobronchial tree, TBLB is performed. Advance the scope until it reaches the diseased segmental bronchus of interest. Then the cup shaped biopsy forceps should be passed via the working channel of the FOB. It is advanced to the periphery of the diseased region. Placing the forceps near, but not at the lung surface, decreases the risk of pneumothorax. Next, the forceps is withdrawn approximately 1 cm, jaws are opened and advanced slightly to obtain the sample . The forceps is then advanced to diseased area where resistance was encountered, and the jaws are closed. In case the patient reports pain at this point, the forceps is gently opened and withdrawn. Only the visceral pleura is pain sensitive.The biopsy forceps is firmly retracted to obtain the sample .This is then placed in formalin and sent for histopathologic evaluation.

Number of Biopsy Specimens

BTS recommendation[38]:

- 4 to 6 biopsy samples for diffuse lung disease
- 7 to 8 samples for focal lung disease

In patients with diffuse lung disease, single sample yield is around 53% and 33% of diagnosis were provide with second sampling. In case of sarcoidosis stage (2 and 3) 4 to 6 specimen will provide adequate diagnosis but in stage 1 disease, additional biopsy specimens upto 10 is needed[39]. In a large study, the diagnostic yield from localized lesions increased was 23%

with 1–3 specimens .But if we take 6–10 specimens,the yield increases to 73%.[40].

Specimen Handling

The specimens obtained from the procedure are placed in container filled with 10 % formalin and sent for histo pathological examination. Whenever infections are considered, biopsy material sent to the microbiology lab in Ringer's lactate. The quality of biopsy specimen is difficult to asssess because the size of the tissue fragment is very tiny in the range of 1 to 3 mm. In one study, they proposed that biopsy specimen containing more than 20 alveoli may be considered adequate to diagnosis infective etiology[41]. But subsequent studies showed it is not reliable in all cases, and many physicians still believe diagnostic yield from TBLB depends more on the number of the specimens obtained rather than actual number of alveoli in each biopsy specimen. In another study, they proposed that tissue with alveoli were more likely to float in 10% formalin rather than tissue without alveoli (float sign) but the practical value is still unproven[42]

Pneumothorax and hemoptysis are the important complications but occurs only less than 2 % of patients**.**

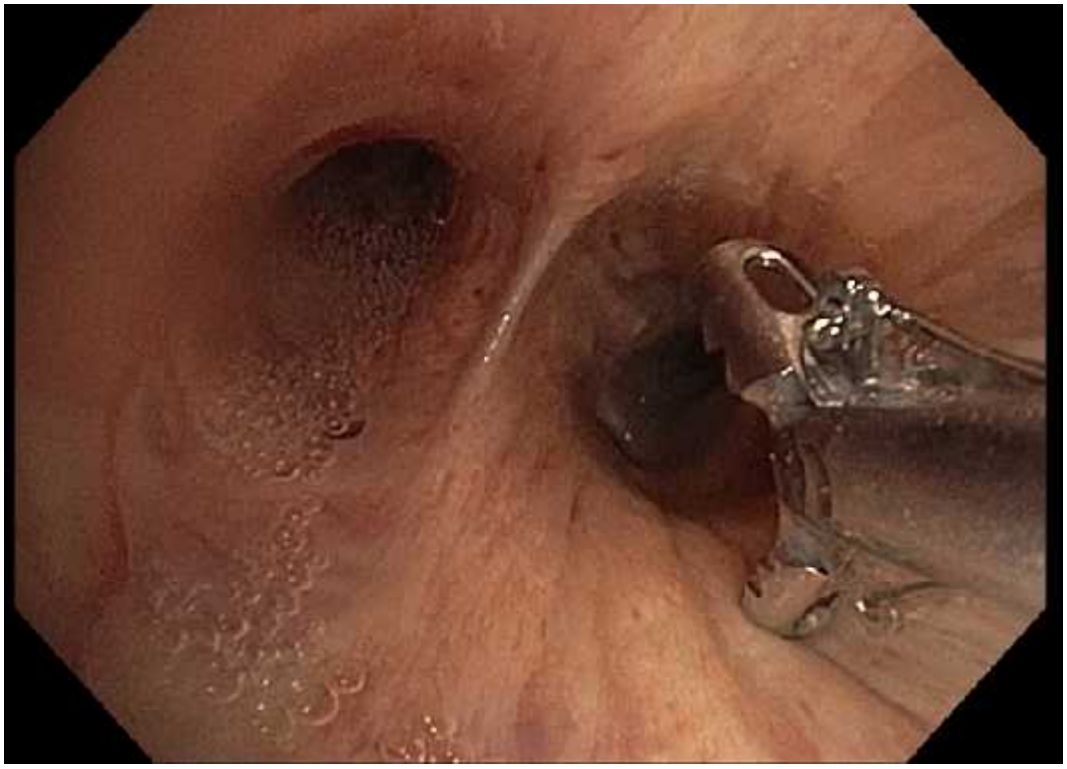


Fig 16: Transbronchial lung biopsy procedure.

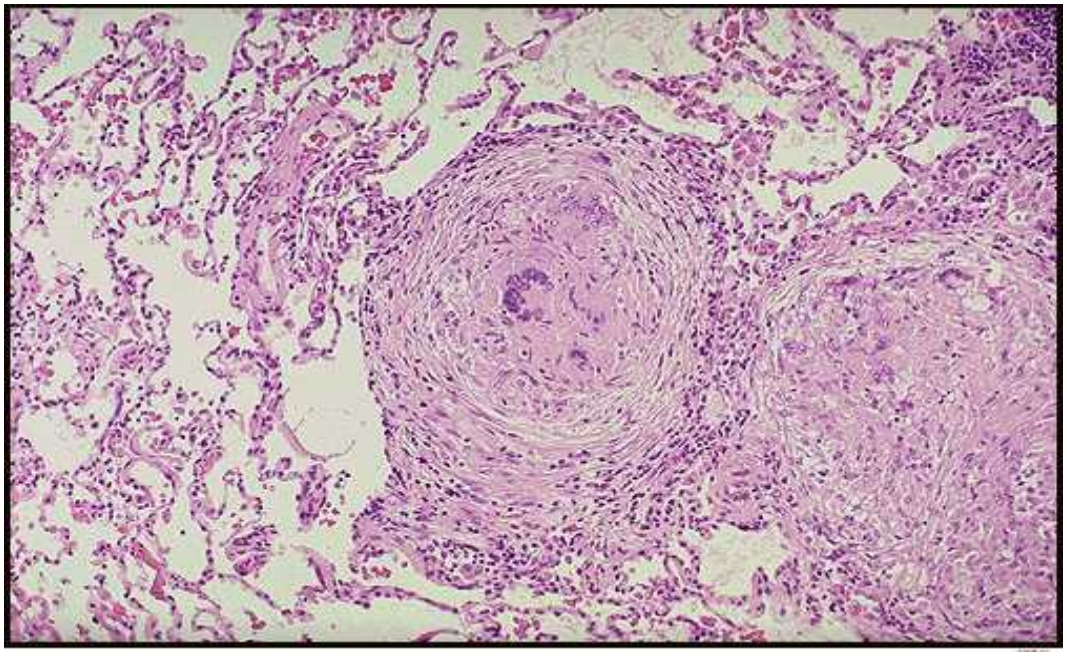


Fig 17 :Histology section of lung biopsy showing Tuberculous granuloma.

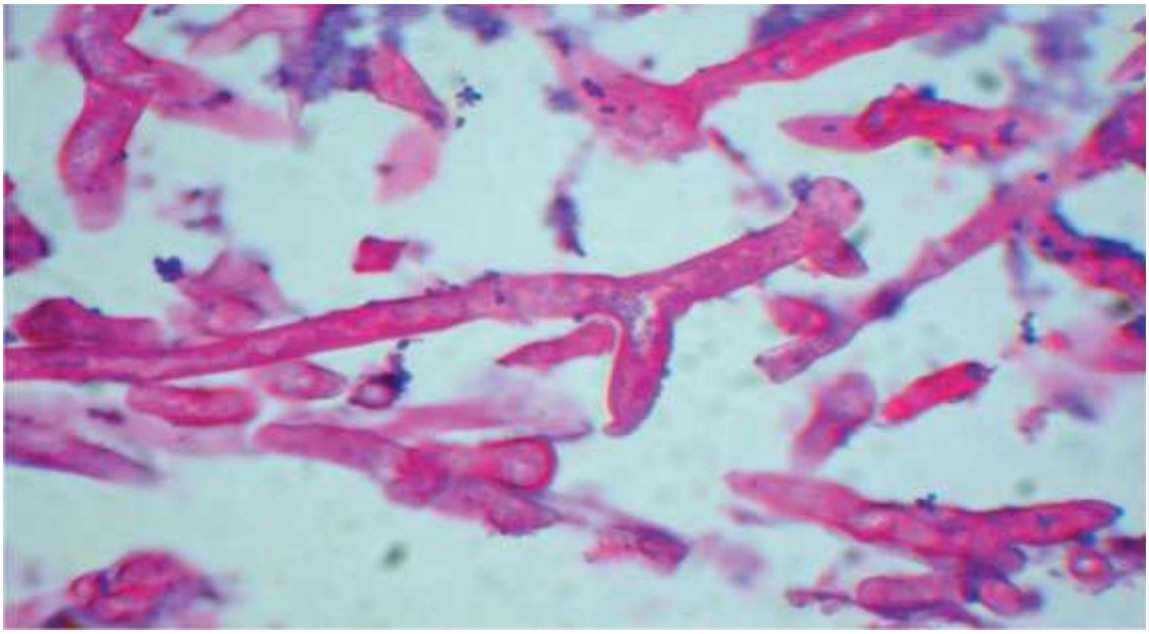


Fig 18:HPE of lung biopsy showing Mucormycosis. It has irregular branching aseptate hyphae.

TBNA:

Transbronchoscopic needle aspiration (TBNA) by using rigid bronchoscope was first reported by Schieppati in 1958. Since 1978 ,fiberoptic bronchoscopy is used for trans bronchial needle aspiration. TBNA is a useful technique for obtaining sample from mediastinal nodes. Hilar lymph nodes, mediastinal mass lesions close to the airways also sampled with this technique. It is a blind procedure. The diagnostic yield is widely variable ranging from 15% to 83%. The yield mainly depends on the size and location of the nodes and operator's experience.

Fig 19: Transbronchial needle aspiration(TBNA) procedure

Fig 20: Cytology smear made from Aspirates.

The needle used for TBNA should be retractable with size between 18 and 22 gauge, length between 13 and 15 mm. Lymph nodes with clear anatomic landmarks (Eg:right lower and left paratracheal mediastinal lymph nodes , subcarinal lymph nodes and hilar lymph nodes) can be adequately sampled .[43]A recent meta-analysis reported a sensitivity of 78% [44].

Overall major complication rate is very less approximately 0.26%. Complications include damage to the working channel of the bronchoscope, fever, and minor bleeding from the puncture site[46].

BRONCHIAL BRUSH

Lesions not reachable by direct biopsy with a forceps can be accessed using bronchial brush. This instrument contains a rigid central wire surrounded by brushes of different size and shape. The brush can be moved to and fro against the nearby tissue, by which samples can be obtained. Minor trauma can occur to the tissues due to brush movement. The collected sample specimens are used for cytological or microbiological analysis. When bronchial brushing is combined with endobronchial biopsy of central lesions, the diagnostic yield of FOB increases between 79% and 96%.

Protected Specimen Brush:

This technique is used to help to arrive at etiological diagnosis in patients with suspected pneumonia. The brush is enclosed within a double catheter sheath using which specimens are collected. The catheter is sealed

at distal end by a wax plug. The plug can be removed easily before obtaining the specimen. The catheter sheath and wax plug is to prevent contamination of the brush with nasopharyngeal flora, that remain inside the working channel of the bronchoscope.

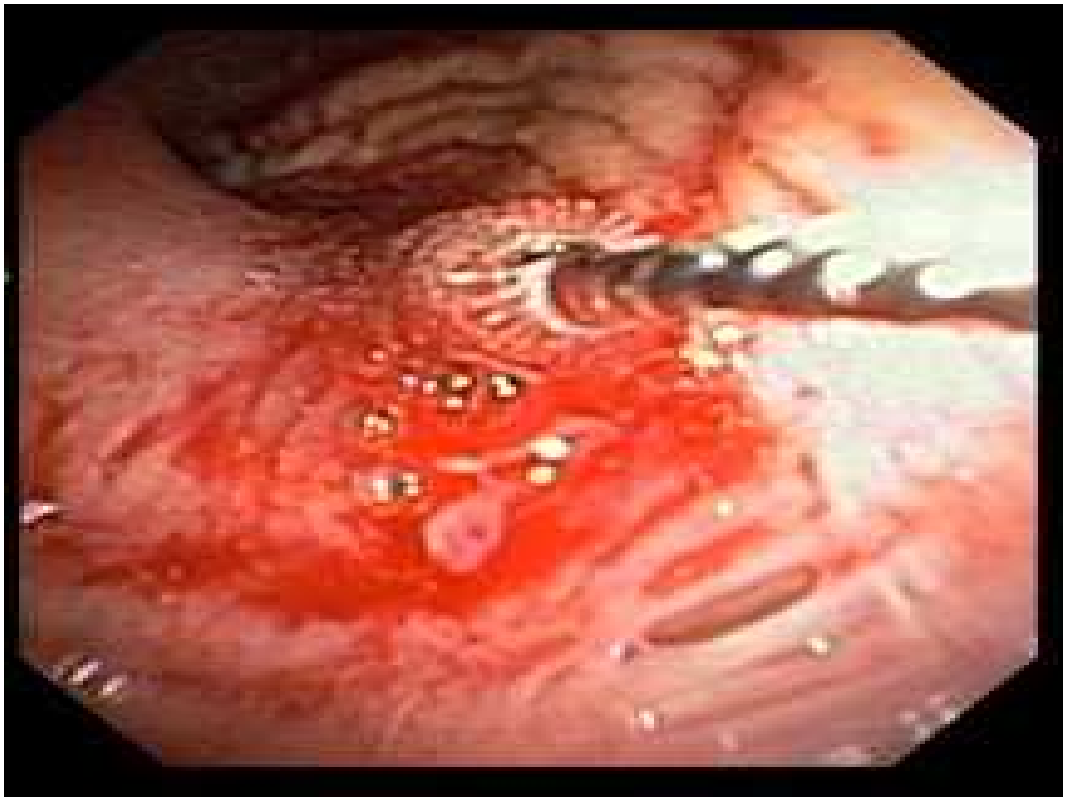


Fig 21: Bronchial brushing procedure.

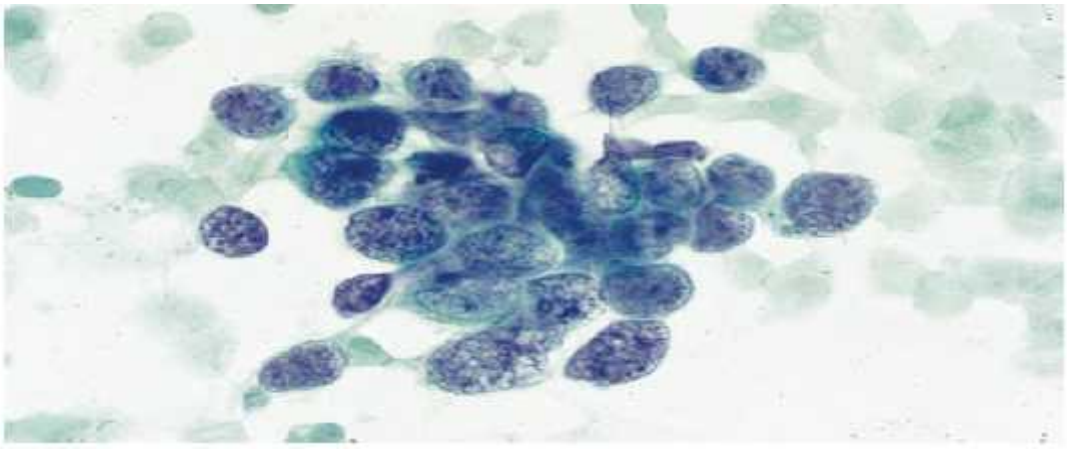


Fig 22 : Brush cytology smear of small cell carcinoma showing tightly packed cells with well preserved powdery chromatin texture .

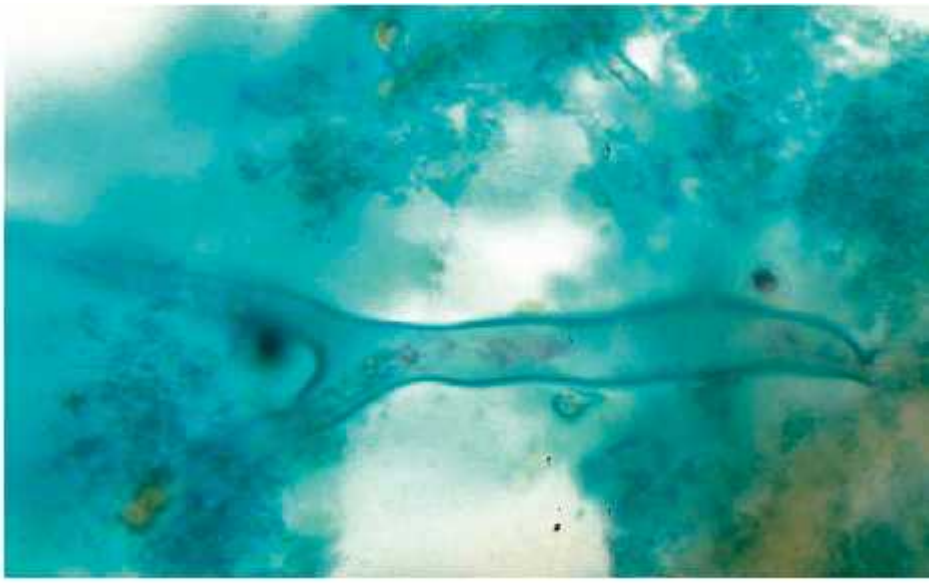


Fig 23: Bronchial brush cytology MUCORMYCOSIS:characteristic branching, ribon like hyphal fragments without septa .

A prospective observation study was conducted by Mohammed El Shabrawy et al[47] in Department of Chest medicine, Zagazig University,Egypt from Sep 2013 to Feb 2015.A total of 135 patients with NRP were included in the study.Patients were subjected to FOB and BAL.Most common cause of NRP in their study was pyogenic infections 113 (83.7%) followed by malignancy in 18 (13.5%) and TB in 4 (2.9%)patients.BAL fluid cytology was positive in 33.3% of patients. TBLB was positive in 55.5% , bronchial brush was positive in 16.6% of patients. Among infections, Klebsiella pneumoniae was the most common organism isolated in 29 (24.8%) patients followed by Pseudomonas (19.65%) and Streptococcus pneumoniae (19.65%).Predominant site of involvement was right upper lobe in 25.9% of patients. They reported diabetes mellitus was most common co morbidity associated with non resolving pneumonia.

Bhupendra Kumar Jain et al[48] studied the role of FOB and CT guided FNAC in diagnostic evaluation of non resolving pneumonia.Sixty five consecutive patients with non resolving pneumonia admitted under respiratory medicine unit were subjected to FOB.In patients where FOB result was inconclusive,CT guided FNAC was done. The most common cause for non resolution found in this study was pyogenic bacterial infections in 24(37%)patients ,followed by TB 19(29.2%), bronchogenic carcinoma in 15(23%) patients and others.Among infections Streptococcus

pneumoniae (50%)was the most common bacteria isolated Pseudomonas, Klebsiella, Legionella, Aceitnobacter, Staphylococcus were isolated in rest of patients. Squamous cell variety was the predominant carcinoma detected in their study accounting for eight out of 15 malignancy cases. Smoking, alcoholism, diabetes and bronchiectasis were significantly associated with non resolution($p<0.5$). Right upper lobe was the most common site involved in 25% patients. The overall diagnostic yield of FOB was 81%.In patients with inconclusive results from FOB, CT guided FNAC was done. They concluded that FOB should be the first option in evaluating NRP before CT guided FNAC.

Arunabha D Chaudhri et al,[49] conducted a prospective, observational study in a tertiary care hospital involving 60 patients with non resolving pneumonia .The efficacy of FOB and CT guided FNAC in arriving at etiological diagnosis was studied. FOB was useful as a diagnostic tool in 85.7% of patients. Pyogenic infection (53.3%) was the most common etiology followed by bronchogenic carcinoma in 26% and TB in 16.7% of cases. Among infections, Klebsiella species were isolated in 13 cases followed by Pseudomonas in 11 cases.Right lung particularly, right upper lobe (25%) was most commonly affected in NRP. Bronchogenic carcinoma accounted for 16 cases, out of which predominant variety was squamous cell carcinoma found in 10 cases followed by adenocarcinoma in 5 patients.

Seven out of ten cases of squamous cell cancer was diagnosed by bronchoscopy whereas all cases of adenocarcinoma was diagnosed by CT guided FNAC . Multilobar or bilateral involvement was common in TB patients (80%).CT guided FNAC was done in patients with inconclusive results from FOB and in those who did not give consent for FOB. Combined yield of FOB and CT guided FNAC was 98.33%.They concluded that FOB is a safe and very useful procedure and should be the first investigation of choice before CT guided FNAC in evaluation of NRP.CT guided FNAC is a good procedure , especially for peripherally situated lesions.

Jayaprakash et al,[50] studied the etiology and clinical outcome of NRP in tertiary care institute,Kerala. Study design was prospective observation study.Out of 821 patients admitted with pneumonia,70 patients with NRP were studied.Tuberculosis, 25 (35.7%) was the most common etiology followed by malignancy in 19 (27.1%) cases, infections with drug resistant organism in 10 (14.3%) patients, Pneumocystis pneumonia in 7.1% and BOOP in 5.7% of patients. Adenocarcinoma (42.1%) was the most common among malignancies. Klebsiella species (60%) was the most common pathogen among infections.Most common risk factor associated with non resolution of pneumonia was smoking (60%).Other statistically significant comorbities were diabetes mellitus,COPD and hypertension.

A Prospective observation study was done by Batau Bhadke et al,[51] in 2010 to study the utility of FOB as a diagnostic tool in NRP.120 subjects who satisfied inclusion criteria underwent FOB procedure.FOB was diagnostic in 90(75%) patients. Bacterial pneumonia were found in 32(26.6%) patients,malignancy in 28(23.3%),pulmonary TB in 20(16.6%),fungal pneumonia in 6(5%) and foreign bodies in 4(3.33%) patients. Streptococcus pneumoniae was the most bacterial etiology found in 16(50%) patients followed by Staphylococcus in 10(31.25%) and Klebsiella in 6 (18.75%) patients.

Etiology and clinical profile of patients with NRP attending OPD, chest hospital in Visakhapatnam was studied by Vipparthi Surya Kumari et al,[52].A total of 32 patients with NRP were subjected to FOB, lung FNAC and CT chest .TB (33.3%)followed by malignancy (30.3%) and infections (16.6%) were the common etiologies for non resolution found in the study. Squamous cell carcinoma and adenocarcinoma were the common malignancies detected.Among infective cause, commonest organism identified was Klebsiella (57.14%) followed by Pseudomonas (28.5%) and E.coli (14.2%). Diabetes (23.3%) was the most common co-morbidity associated with nonresolving pneumonia in the study followed by COPD (20%), and Hypertension (16.6%).

Nimit V Khara et al,[53] studied the diagnostic yield of FOB in 3 common lung conditions -pneumonia, TB and lung cancer. A total of 289 patients were included in study. The overall diagnostic yield of FOB was 55.7% .The yield of FOB in diagnosing pulmonary TB was 37.7%.The diagnostic yield was 48.7% and 68.5% in pneumonia and lung cancer respectively. They also found FOB guided BAL fluid analysis was very useful in diagnosis and identification of the causative organism in patients with non-resolving and hospital acquired pneumonia.

Amit J Asari et al,[54] conducted a retrospective observation study in a tertiary care hospital, Ahamedabad. The primary objective of their study was to study the yield of FOB in diagnosis of NRP.A total of 34 patients were studied . Pyogenic infection was the most common etiology in 19 cases(55.88%) followed by bronchogenic carcinoma 8 cases (23.5%),TB in 6 cases(17.6%).Among infections, most frequent organism isolated was Streptococcus pneumoniae in 8 patients (42.1%).Among malignancies, the most common histological pattern was adenocarcinoma 4 (50%) followed by squamous cell carcinoma 25%,small cell 12.5% and large cell carcinoma. The importance of FOB with BAL in diagnosis of sputum smear negative pulmonary TB was studied by Novin Nikbhash et al,[55] from Iran. A total of 290 sputum smear negative TB patients between the years 2006 and 2012 were studied. All patients were subjected to FOB,BAL stain and culture.Out

of 290 patients, BAL smear detected TB bacilli in 110 patients.Even in patients in whom BAL smear was negative,BAL culture grew TB bacilli in 64 (35.5%) patients.Study concluded that FOB guided BAL is a rapid and useful technique to establish definitive diagnosis in patients with sputum smear negative TB .

The yield of FOB with BAL in association with chest CT findings and symptoms in immune compromised patients was studied by Kyle R Brownback et al,[56]. The study included a total of 133 subjects.The study population included were those on immunosuppressant therapy,retro positive individuals,neutropenics and hematopoietic stem cell, organ transplant recipients. The diagnostic yield of FOB was 52.7%. Infections particularly viral were the most common etiology found in 38(48.1%)patients followed by bacterial in 9(11%),invasive Aspergillosis in 14(17.7%) and Pneumocystis jiroveci in 6 (7.6%) patients. They concluded that symptomatic patients were more likely to have diagnosis. Significantly higher diagnostic yield was demonstrated in patients in whom, imaging confirmed abnormalities within alveoli or airways .There was also better diagnostic yield with BAL performed in lower lobes compared to middle and upper lobes

MATERIALS AND METHODS

STUDY TITLE

The present study ‘‘**ROLE OF BRONCHOSCOPY TO DETERMINE THE ETIOLOGY OF NONRESOLVING PNEUMONIA IN A TERTIARY CARE INSTITUTE’’** was conducted in Department of Thoracic Medicine, Tirunelveli Medical College, Tirunelveli after obtaining approval from Tirunelveli Medical College Institutional Ethical Committee(TIREC).

AIMS AND OBJECTIVES

- To find out the etiology of non resolving pneumonia by using Bronchoscopy .
- To study the role of bronchoscopy in non resolving pneumonia.

STUDY DESIGN:

Prospective observational study

STUDY PLACE:

Department of Thoracic Medicine, Tirunelveli medical College and hospital

STUDY PERIOD:

From June 2015 to August 2016

STUDY POPULATION:

Adults (≥ 12 years) admitted with non resolving pneumonia in Thoracic medicine ward,Tirunelveli Medical College Hospital during the study period

INCLUSION CRITERIA:

Patients who fulfill the criteria of non resolving pneumonia.(patients who presented with pneumonia like syndrome and the radiograph has failed to resolve by 50% in 2 weeks, or completely in 4 weeks , or does not show significant radiographic resolution after at least 10 days of antibiotic therapy)

EXCLUSION CRITERIA:

1.Unwilling patients.

2.Known case of lung cancer

3.Known case of Sputum positive tuberculosis

4. Patients with poor general condition, hemodynamic instability, uncooperative patients.

5.Recent myocardial infarction

METHODOLOGY:

After obtaining approval from ethical committee, a total of 68 patients who fulfilled the study criteria were enrolled for the study. Name, age , sex, residence, occupation of all patients were noted. Detailed clinical history was taken. Duration of symptoms, prior history of ATT ,associated co morbities like Diabetes, Hypertension, Coronary artery disease were recorded. History of smoking, alcoholism was noted .Laboratory investigations like complete blood count, Random blood sugar, Renal function test, Liver function test was done. Patients were tested for HIV, hepatitis B, hepatitis C serology, Sputum for AFB(at least 3 samples) were taken before procedure. Sputum for Gram stain and culture, fungal stain and culture ,sputum cytology for malignant cells were sent. Chest xray and CT chest were taken in all patients . Further investigations like USG chest, USG guided FNAC, cardiac evaluation, Serological test were done as needed. Before the procedure, all patients were treated with empirical antibiotics at least for 10 days according to the standard guidelines .

Bronchoscopy procedure, benefits, complications were explained clearly to the patients in their local language and consent(oral &written) was obtained .Patients pulse rate, respirator rate ,blood pressure, oxygen saturation were recorded before the procedure. Olympus BF-TE 2 model conventional Fiberoptic bronchoscope was used for the study .It has 120

degree field of view so that it provides broader view. Tip has bending range of 130 degree upward and 180 degree downwards. It has 2.8 mm diameter and 600 mm length of working channel which allows better instrumentation. For trans bronchial lung biopsy, Olympus FB -231 D type of standard oval shaped biopsy forceps was used. It has 5 mm cup opening and a 115 cm of working length. The Olympus BC-202D-3010 model bronchial brush with covered sheath was used .Brush was 10 mm in length and 3mm in outer diameter Bristle diameter is 0.064mm in length.

During Bronchoscopy, gross inspection of upper respiratory tract, visualisation of vocal cord movements ,tracheo bronchial tree inspection followed by FOB guided procedures were done. Vitals and oxygen saturation was monitored throughout the procedure. All procedures were carried out according to standard guidelines and under universal precautions.

Samples collected were sent immediately to lab.BAL fluid was centrifuged at 1500 rpm for five minutes .Then smear stained with hematoxylin and eosin stain and then cell count ,and cytology analysis were made .BAL fluid was also sent for AFB, Gene Xpert, Gram stain and culture, Fungal stain and culture. Samples obtained from bronchial brushings were sent for cytology .Transbronchial lung biopsy specimen was preserved in formalin and sent for Histopathological examination. USG guided FNAC was done in patients with inconclusive results from FOB procedure.

After the procedure, patients were observed for at least one hour for any complications like massive Hemoptysis or hypoxia. Post procedure chest xray was taken to rule out Pneumothorax.

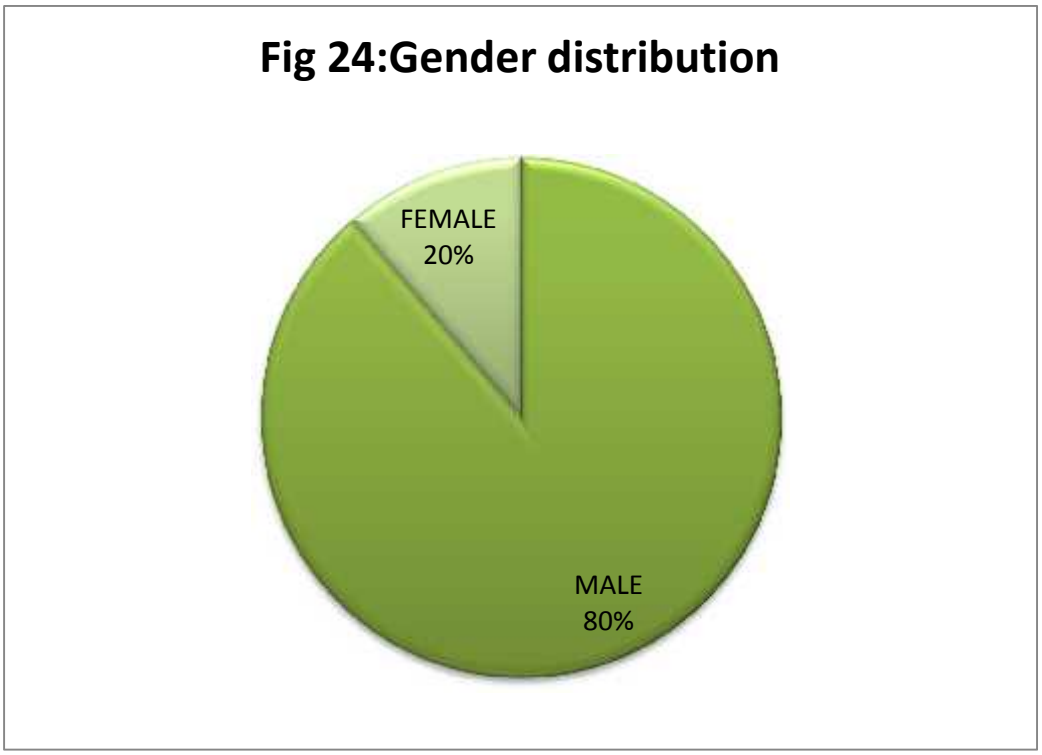
RESULTS

SAMPLE SIZE:

Sixty eight(N = 68) Patients who fulfilled the study criteria were included in the study.

GENDER DISTRIBUTION:

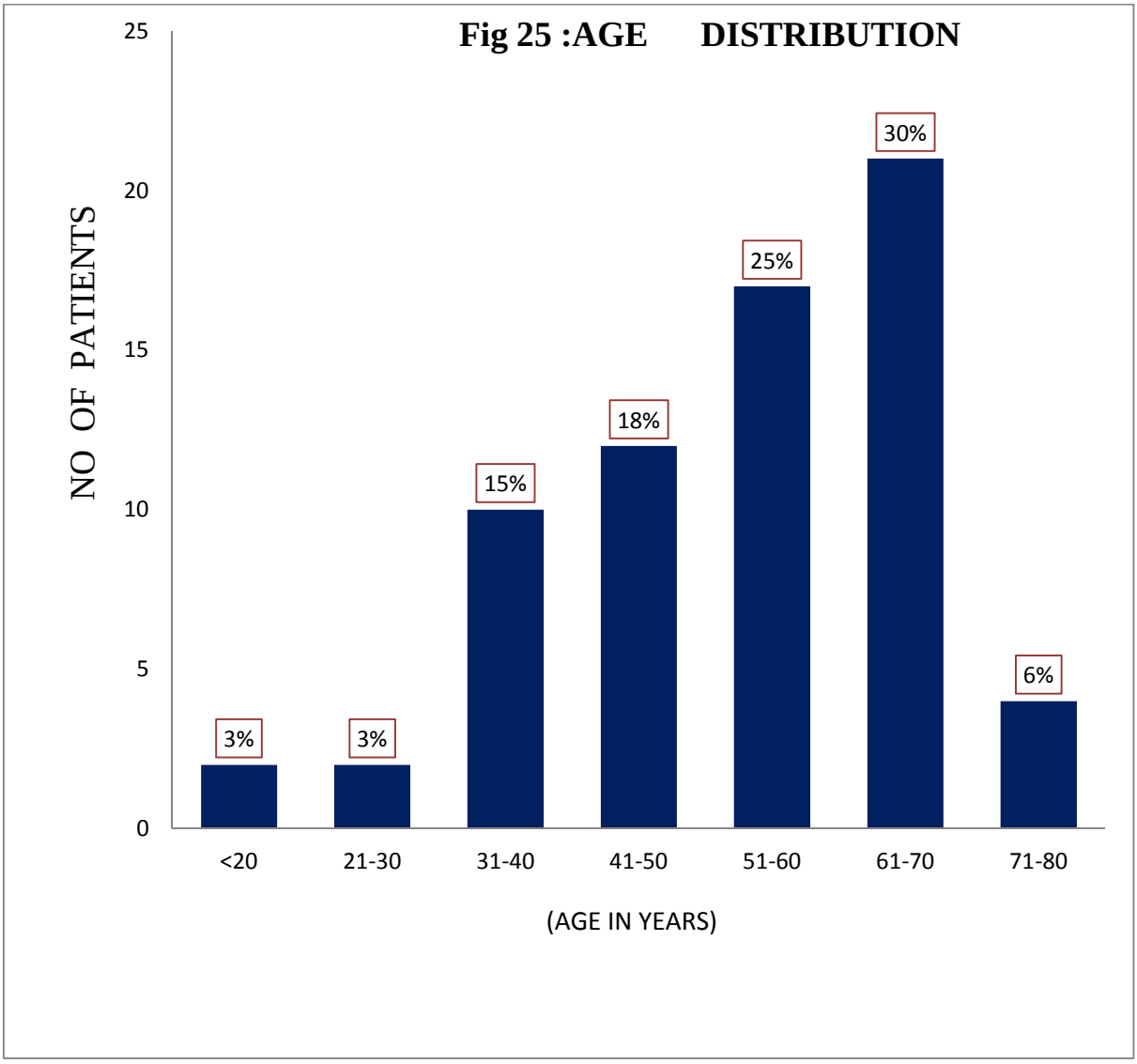
Of the 68 Patients included in the study, majority of the patients were males 80%(n=54). Females were 20% (n= 14). [Fig 24]



AGE DISTRIBUTION:

3%(n=2) patients were between 15-20 years, 3%(n=2) were between 21-30years, 15%(n=10) were between 31-40 years , 18% (n=12) were between 41-50 years, 25%(n=17) were between 51-60 years , 30%(n=21) were between 61-70 years and 6% (n=4) were between 71-80 years age.[Fig 25]

In my study ,majority of patients were above 50 years of age.



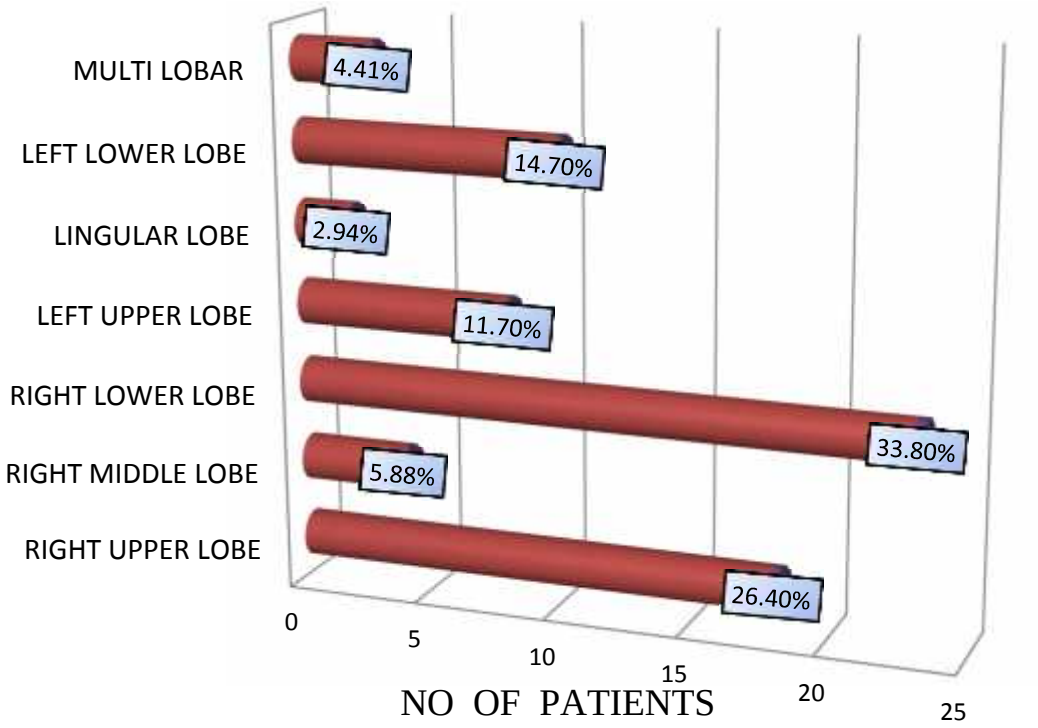
CT-CHEST PATTERN

Computerised tomography of patients with non resolving pneumonia showed varied distribution. Majority of the patients with non resolving pneumonia had lesions affecting right lower lobe 33% (n=23) followed by lesion distributed in right upper lobe 26%(n=18).Non resolving consolidation was seen in left lower lobe in 14% (n=10) of patients and left upper lobe in 11%(n=8)of patients. Lingular segment was affected in 3%(n=2) of patients. Multi lobar distribution of consolidation were seen in 4%(n=3).[Fig 26]

TABLE 2: CT CHEST PATTERN IN MY STUDY.

CT CHEST PATTERN	NO OF PATIENTS (n – 68)	PERCENTAGE
Right upper lobe	18	26.4%
Right middle lobe	4	5.88%
Right lower lobe	23	33.8%
Left upper lobe	8	11.7%
Lingular lobe	2	2.94%
Left lower lobe	10	14.7%
Multi lobar	3	4.41%

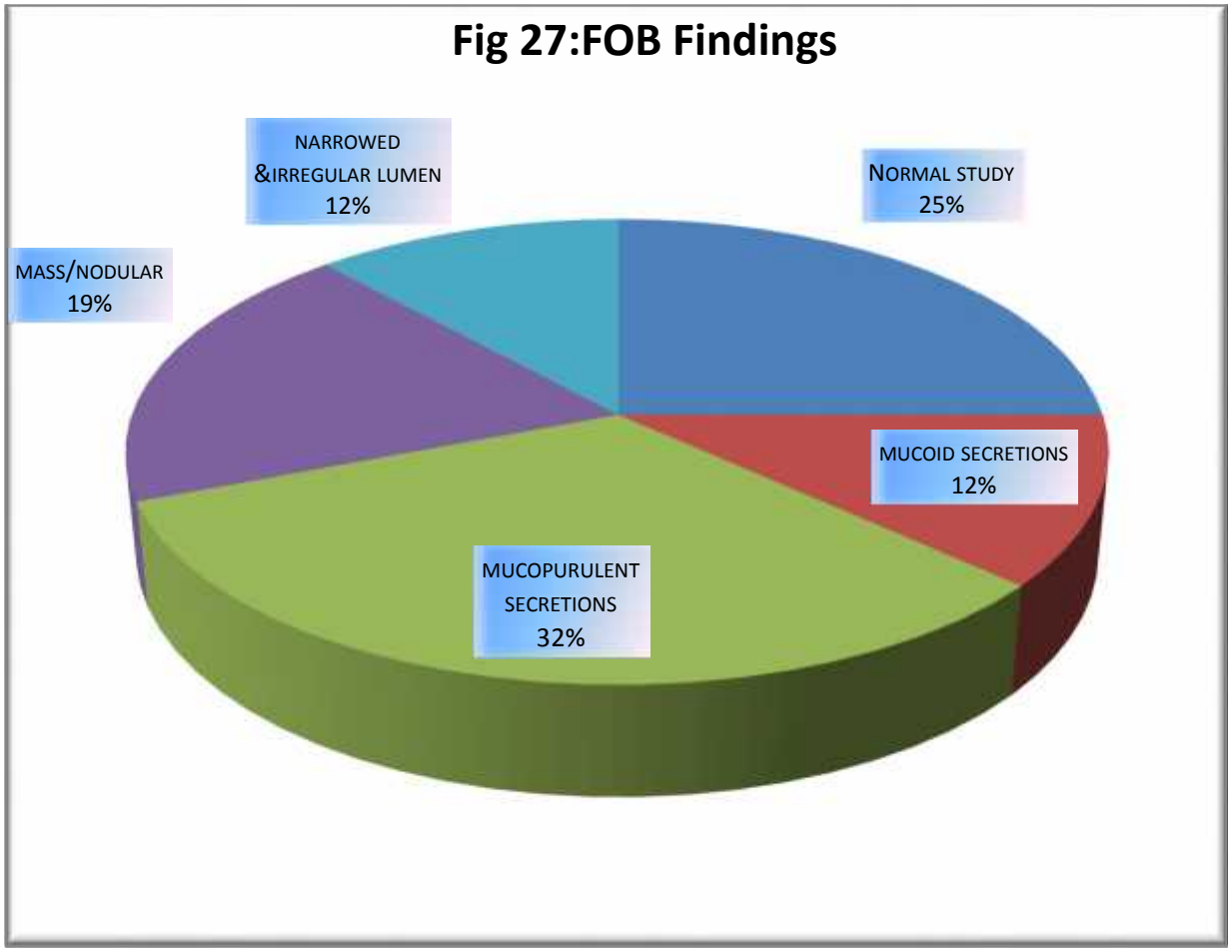
Fig 26:CT CHEST PATTERN



FOB findings :

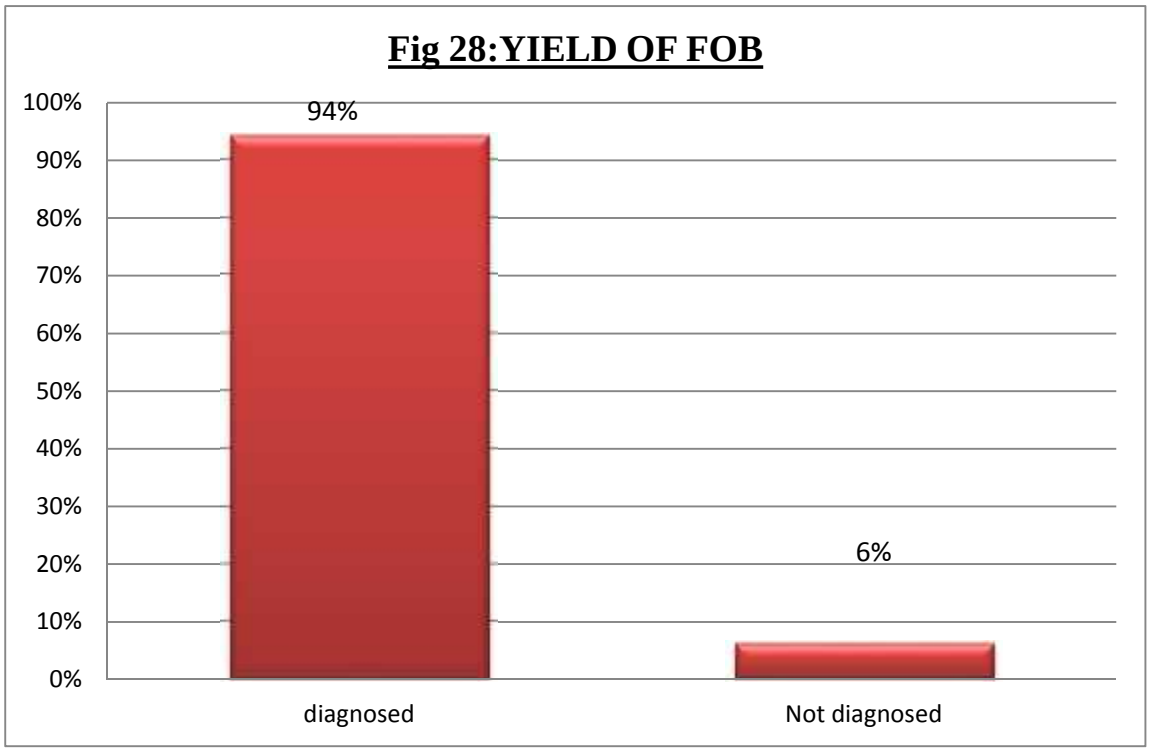
FOB showed various findings during gross inspection of tracheobronchial tree. In 25%(n=17) of patients FOB study was normal. Inflammed mucosa along with mucopurulent secretions was noted in 32%(n=22) of patients. In 19% (n=13)of patients visible endobronchial mass lesion or nodular lesions were seen. In 8%(n=) of patients mucoid secretions and in few patients mucoid impaction were noticed and in remaining 8% of patients, bronchial segments were irregular, inflammed and narrowed.[Fig 27]

Even though 25 % of patients showed normal study during the procedure,FOB guided procedures revealed the etiology in them.



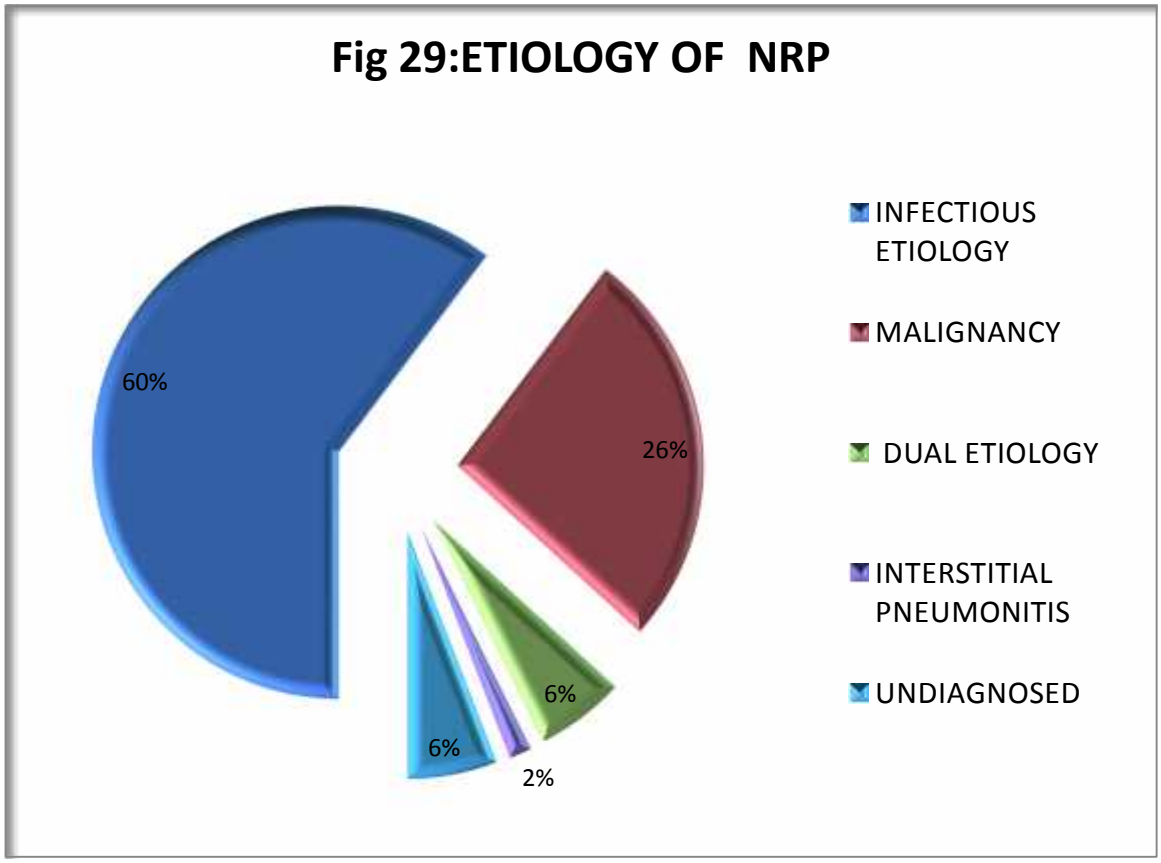
DIAGNOSTIC YIELD OF FOB:

Overall diagnostic yield of FOB in my study was 94%(n=64).[Fig 28].In 3 out of 4 patients ,USG guided FNAC was carried out which revealed diagnosis. In remaining 1 patient diagnosis could not be made.



ETIOLOGY OF NONRESOLVING PNEUMONIA:

Majority of cases diagnosed in my study was infectious diseases followed by malignancy. In my study, infections is the cause for non resolution in 60.29% (n=41) of patients . In 26.47% (n=18) of patients malignancy was the etiology. Combined etiology was noted in 5.88%(n=4)and Interstitial pneumonitis was diagnosed in 1%(n=1).[Fig 29]



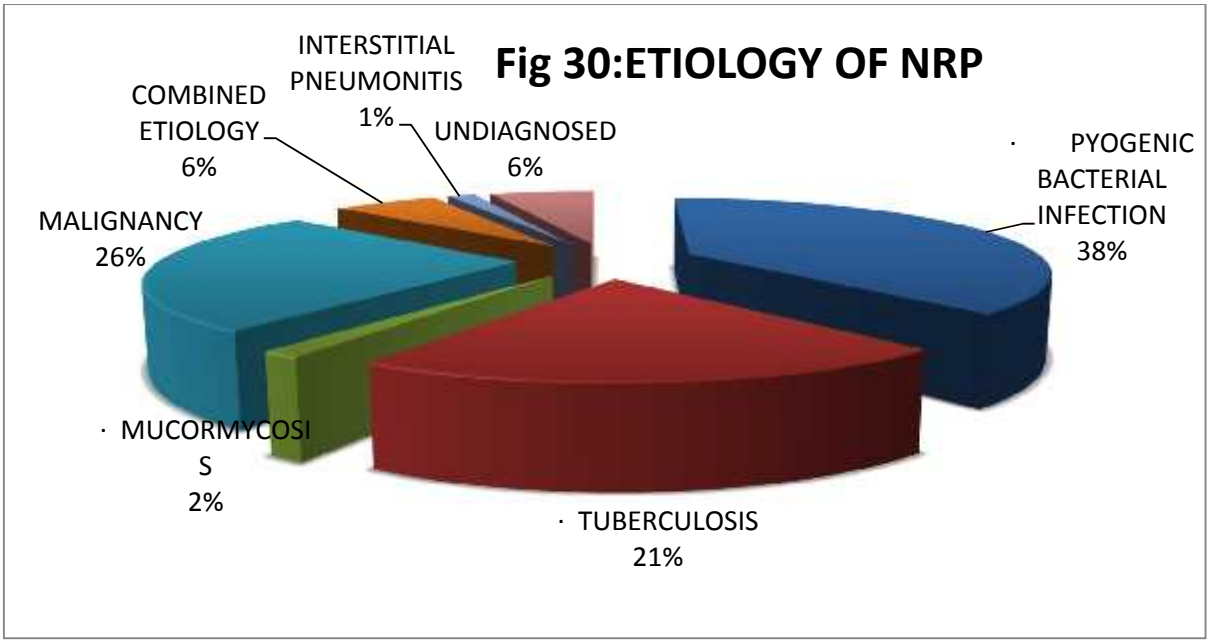
- Among the infectious causes,Gram negative pyogenic bacterial infection was diagnosed in 41.1%(n=28).Tuberculosis was diagnosed in 25% (n=17) and fungal infection - Mucormycosis was diagnosed in 1%(n=1).[Fig 30]
- Klebsiella species is the predominant bacterial infection identified followed by pseudomonas infection.

TABLE 3: YIELD OF FOB IN NRP

Yield of FOB	Frequency(n=68)	Percentage
Infectious etiology ⟩ Pyogenic bacterial infection ⟩ Tuberculosis ⟩ Mucormycosis	 26 14 1	60.29%
Malignancy	18	26.47%
Combined etiology	4	5.88%
Interstitial Pneumonitis	1	1.47%
Undiagnosed	4	5.88%

⟩ Among the Malignancy, Squamous cell carcinoma was the predominant type followed by Adenocarcinoma and small cell carcinoma.

⟩ Dual etiology was diagnosed in 4 patients. Squamous cell carcinoma along with tuberculosis was diagnosed in 2 patients. Another patient, Squamous cell carcinoma combined with secondary bacterial (klebsiella species) infection was diagnosed. In another patient tuberculosis and coagulase negative staphylococcus aureus was diagnosed.



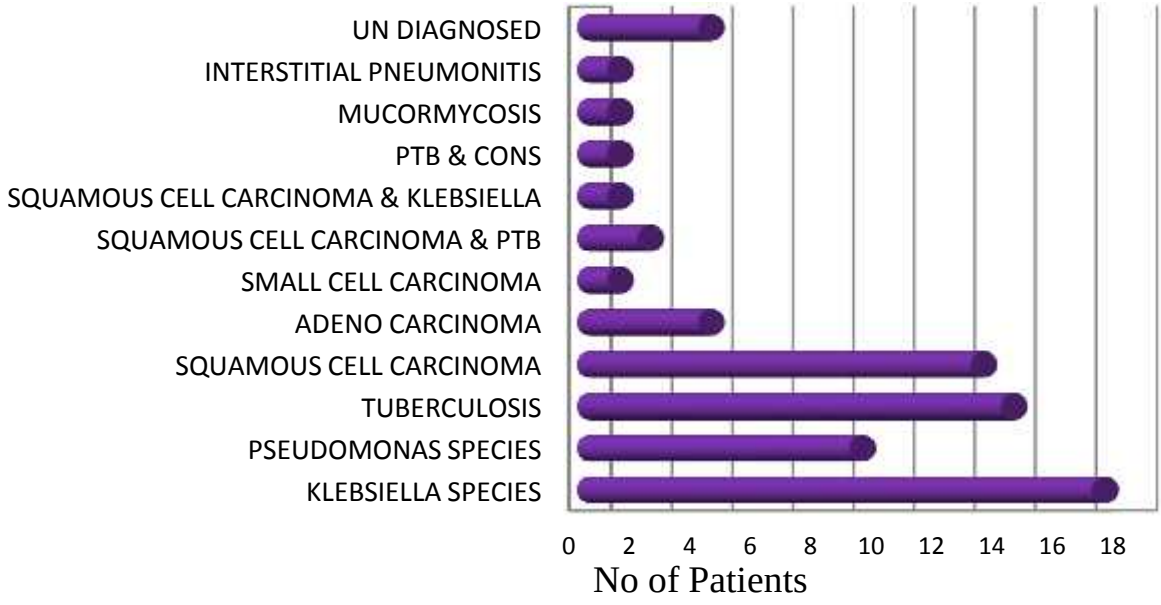
OVER ALL DIAGNOSIS

Various etiologies diagnosed in my study is summarised in table(4).[Fig 31]

TABLE 4:DIAGNOSIS OF NRP IN MY STUDY

DIAGNOSIS OF NRP	NO OF PATIENTS (n=68)	% PERCENTAGE
Klebsiella Species	17	25%
Pseudomonas Species	9	13%
Tuberculosis	14	20%
Squamous Cell Carcinoma	13	19%
Adeno Carcinoma	4	6%
Small Cell Carcinoma	1	1%
Squamous Cell Carcinoma & PTB	2	3%
Squamous Cell Carcinoma & Klebsiella	1	1%
PTB & CONS	1	1%
Mucormycosis	1	1%
Interstitial Pneumonitis	1	1%
Un diagnosed	4	6%

Fig 31:over all etiology of NRP



BRONCHOALVEOLAR LAVAGE ANALYSIS:

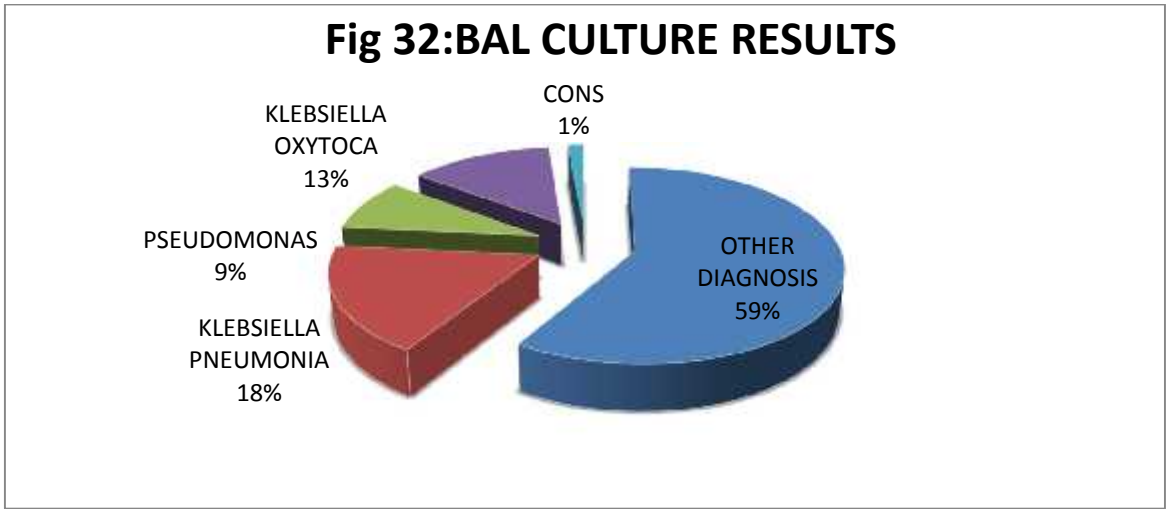
BAL CYTOLOGY:

BAL fluid cytology revealed malignancy in 9%(n=6) of patients. In remaining 91% nonspecific inflammatory changes was observed.

BAL FLUID MICROBIOLOGICAL ANALYSIS:

- Out of 68 patients, in 28 patients BAL culture revealed bacterial infection. Klebsiella pneumoniae was the predominant organism[17%(n=12)] followed by Pseudomonas aeruginosa(13%)(n=9).Klebsiella oxytoca was identified in 9%(n=6) and Coagulase negative Staphylococcus aureus identified in 1%(n=1) of patients.[Fig 32]

- Pyogenic bacterial infections was the most common etiology observed with Klebsiella species (26%) being the predominant pathogen.



Diagnosis of tuberculosis

- Tuberculosis was found as the etiology of non resolving pneumonia in 25% (n=17) of patients.
- Out of this , AFB smear cytology was positive in 12 patients. BAL fluid CBNAAT analysis detected Mycobacterium tuberculosis in 5 patients. TBLB revealed caseating granulomas in 5 patients.

FOB guided protected specimen brush results:

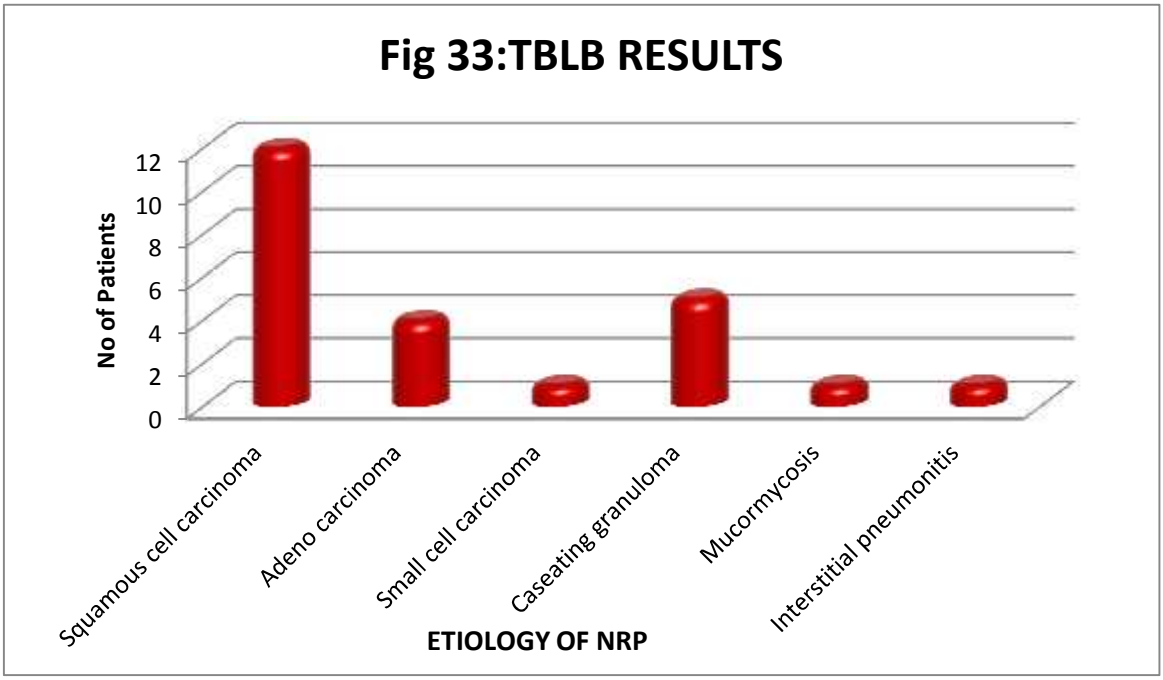
FOB guided brush cytology revealed malignancy in 10 % (n=7) of patients. Squamous cell carcinoma was the diagnosis in 4 patients and in remaining patients brush cytology showed probable malignancy which was confirmed later as squamous cell carcinoma by TBLB HPE reports.

TBLB results:

Out of 68 patients, TBLB was done in 36 patients. Out of which, TBLB diagnosed etiology of NRP in 24 patients. Malignancy was diagnosed in 17 patients. Granulomatous pathology was diagnosed in 5 patients. one case HPE report revealed Mucormycosis infection and another one diagnosed as Interstitial Pneumonitis.[Fig 33]

TABLE 5:Transbronchial lung Biopsy Results.

TBLB RESULTS	**No of Patients (n=24)**	**Percentage**
Squamous cell carcinoma	12	50%
Adeno carcinoma	4	17%
Small cell carcinoma	1	4%
Caseating granuloma	5	21%
Mucormycosis	1	4%
Interstitial pneumonitis	1	4%



CO MORBID CONDITIONS:

In my study,out of 68 patients,41.1%(n=28) patients were diabetic and 51.47% were smokers. Diabetes is predominantly associated with infectious etiology. Other comorbidites were CKD (n=8),post renal transplant (n=1) and CA esophagus(n=1).Apart from this, COPD,CAD,OLD CVA,Hypertension were other co morbidities.[Fig 34]

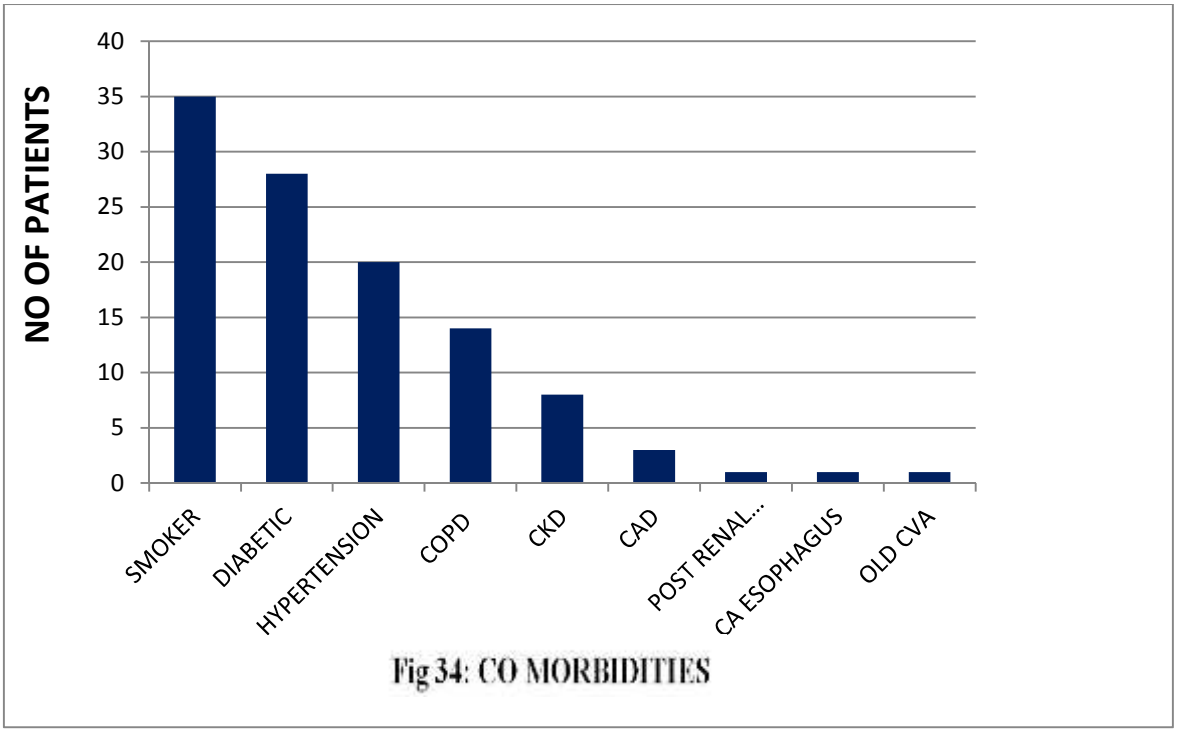


Fig 34: CO MORBIDITIES

COMPLICATIONS:

Following FOB, chest X ray was taken in all patients. None of them had complications like pneumothorax. Only minor complications like transient fever, minor bleeding, transient desaturation during the procedure were noticed.There was no other major complications like massive hemoptysis .

DISCUSSION

The present study included 68 patients with non resolving pneumonia. All patients were subjected to Bronchoscopy .Out of 68 , etiological diagnosis was made in 64 patients. USG Guided FNAC was done in remaining 4 Patients and diagnosis was made in 3 patients. However, no etiology could be determined in one patient.

Diagnostic yield of FOB to determine the etiology of NRP in my study was 96%(n=64)which is comparable to other studies. In the study done by Chaudhri et al[49], yield of FOB in NRP was 85.7% in the study done by Bhupendra Kumar Jain et al[48] ,diagnostic yield of FOB was 81%. Batau Bhadke et al[51], concluded FOB was diagnostic in 75% of NRP cases. In study conducted by Asari et al[54], the diagnostic yield of FOB was 87% in NRP. Nimit V Khara et al[53], studied diagnostic yield of FOB in 3 common lung conditions(pneumonia,TB and lung cancer) and concluded overall yield of FOB was 55.7% .

TABLE 6 :YIELD OF FOB IN NRP- COMPARISON OF STUDIES

	Yield of FOB in NRP
My study	**96%**
Chaudhri et al	**85.7%**
Bhupendra kumar jain et al	**81%**
Batau bhadke et al	**75%**

In my study majority of the patients were males (80%).Among females, infections (71%) were the most common cause of etiology of NRP when compared to malignancy (28%).Among males ,the major cause of NRP was infections, but incidence of malignancy was higher in males when compared to females probably because of high incidence of smoking habit . Depressed muco ciliary function in smokers is also a risk factor to develop infectious pneumonia.

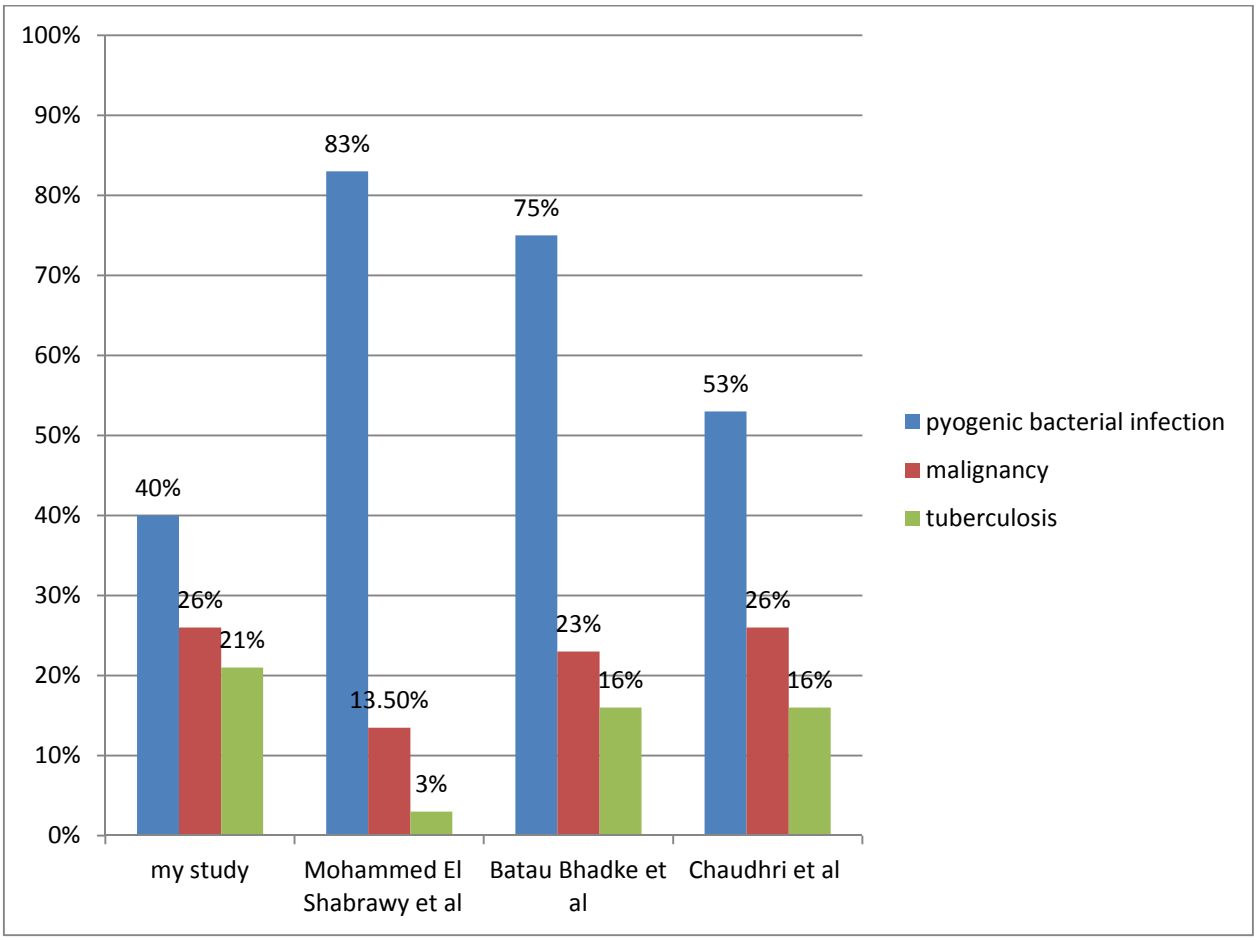
In my study majority of patients were above 50 years of age. The reason was depressed immunity and associated co morbidities more among them when compared to young population.

In CT chest findings, Right lung involvement was more common compared to left side. Right lower lobe (33%) was predominantly involved followed by right upper lobe(26%)and left lower lobe whereas in studies done by Chaudhri et al[49],Bhupendra Kumar Jain et al[48],Mohammed et al [47], right upper lobe involvement was more common.

Muco purulent secretions(32%) was noted in majority of patients during gross inspection of tracheo bronchial tree. Around 25% of patients showed no significant findings during gross inspection, but various FOB guided procedure revealed specific diagnosis in them.

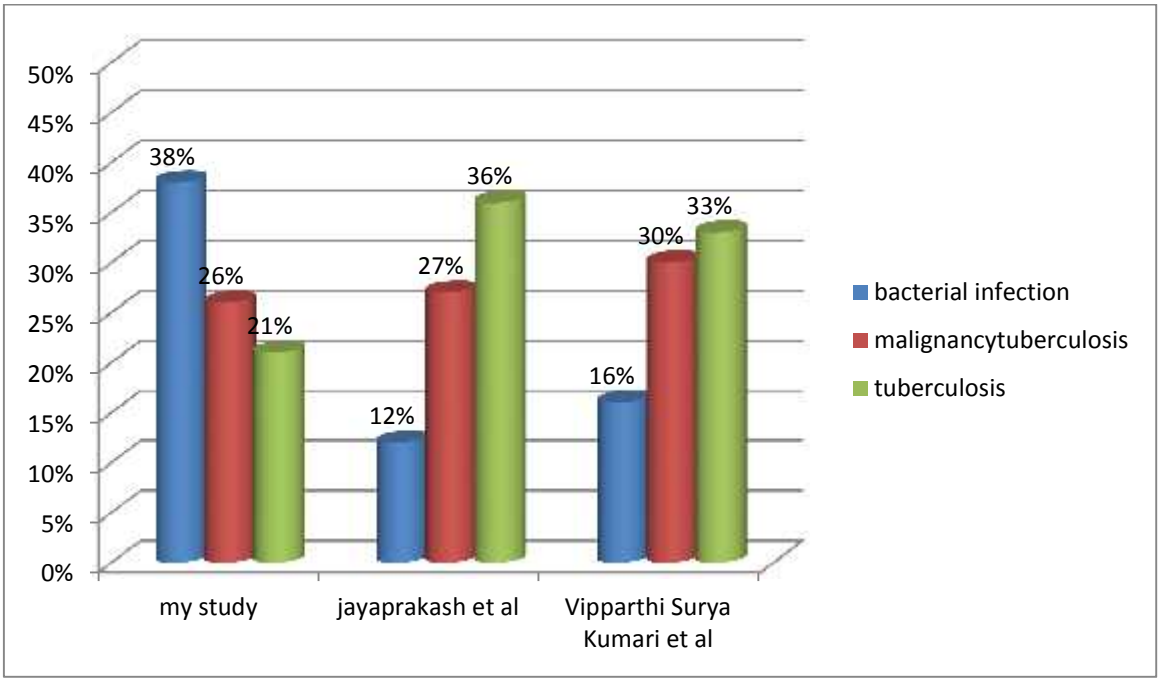
Most common etiology of NRP in my study was Pyogenic bacterial infection (38%) followed by malignancy(26%) and Tuberculosis(21%),which is comparable to other studies. Studies conducted by Mohammed El Shabrawy et al[47] , Batau Bhadke et al[51] , Chaudhri et al[49] ,and Amit J Asari et al[54], concluded pyogenic bacterial infection was the most common etiology of NRP followed by malignancy and tuberculosis .[Fig 35]

Fig 35:ETIOLOGY OF NRP IN VARIOUS STUDIES



In contrast , study done by Jayaprakash et al[50] concluded, TB was the most common etiology followed by malignancy. In Visakhapatnam, Vipparthi Surya Kumari et al[52] ,also concluded similar results .[Fig 36]

Fig 36: ETIOLOGY OF NRP IN VARIOUS STUDIES



Among the bacterial infections , Klebsiella species was most common cause followed by Pseudomonas and CONS which is comparable to other studies. Study done by Mohammed El Shabrawy et al[47], revealed Klebsiella pneumoniae was the most common organism isolated in 29 (24.8%) patients followed by Pseudomonas (19.65%) and Streptococcus pneumoniae (19.65%).Vipparthi Surya Kumari et al[52] ,concluded in his study, most common pathogen identified was Klebsiella (57.14%) followed by Pseudomonas (28.5%) and E.coli (14.2%)

Chaudhri et al[49] , reported Klebsiella species were isolated in 13 cases followed by Peudomonas. All the above quoted studies showed Gram negative organisms were the predominant cause of non resolving pneumonia when compared to gram positive organisms.

But, study conducted by Amit J Asari et al[54], found ,most frequent organism isolated was streptococcus pneumoniae (42.1%) and Batau Bhadke et al[51], also found in his study that Streptococcus pneumoniae was the most bacterial etiology found in 16(50%)patients followed by Staphylococcus in 10(31.25%) and Klebsiella in 6 (18.75%) patients. Bhupendra Kumar Jain et al[48] **,** concluded in his study , Streptococcus pneumoniae (50%)was the most common bacteria isolated. when compared to present study, All these studies showed gram positive organisms was responsible in the etiology of non resolving pneumonia. The reason might be due to variation of organisms according to their local epidemiological pattern.

In the study done by Kyle R Brownback et al[56], in immunocompromised individuals, viral infections were the most common etiology found in 38(48.1%)patients followed by bacterial in 9(11%),invasive Aspergillosis in 14(17.7%) and Pneumocystis jiroveci in 6 (7.6%) patients. In the immunocompromised individual the infectious causes

were different from general population as they acquired more atypical organisms and invasive fungal infections because of decreased immunity.

In the study done by Bhupendra Kumar Jain et al [48], Squamous cell variety was the predominant carcinoma which is comparable to my study. Arunabha D Chaudhri et al[49], also concluded in his study that most common cause Squamous cell carcinoma followed by adenocarcinoma .

In contrast, Jayaprakash et al[50], found Adenocarcinoma (42.1%) was the most common among malignancies .Amit J Asari et al [54], reported adenocarcinoma 4 (50%)was more common, followed by squamous cell carcinoma 25%,small cell 12.5% and large cell carcinoma.. In both studies, CT guided FNAC was used as one of the diagnostic procedures which is better in diagnosing peripheral tumours like Adenocarcinoma. Squamous cell carcinoma being a predominant central tumour is better diagnosed by FOB.

In all patients, before the procedure 3 sputum samples were sent for AFB smear to rule out smear positive tuberculosis. Using FOB related procedures tuberculosis was diagnosed in 17 patients with NRP in my study. We utilised AFB smear, rapid diagnostic method CBNAAT and in few patients TBLB to detect Mycobacterium tuberculosis. Use of FOB in diagnosis of sputum smear negative pulmonary TB done by Novin Nikbakshi et al[55] found tuberculosis in 63% of cases. .

So FOB is a very useful procedure to diagnose TB in smear negative pulmonary tuberculosis patients. Combined etiology was found in 4 patients .Squamous cell carcinoma associated with secondary bacterial (Klebsiella)infection was found in one patient. In 2 patients, squamous cell carcinoma was associated with tuberculosis.

SUMMARY

The present study was conducted in department of Tuberculosis & Respiratory Medicine , Tirunelveli medical college which included 68 patients with non resolving pneumonia. All patients were subjected to Flexible fibreoptic Bronchoscopy .Out of 68 patients , etiological diagnosis was made in 94% of patients. Majority of the patients were males and were above 50 years of age. Majority of the patients with non resolving pneumonia had lesions affecting Right lower lobe. Inflamed mucosa along with mucopurulent secretions was noted in majority of patients during gross inspection of tracheobronchial tree.

The overall diagnostic yield of FOB in my study was 94%(n=64). Infections(60%) were the most common cause of non resolving pneumonia followed by malignancy(26.47%) in my study .Combined etiology was noted in 6% and interstitial pneumonitis was diagnosed in 1% patients.

Among the infective causes, Gram negative bacterial infection was predominantly diagnosed in 38% of patients followed by Tuberculosis (21%) and fungal infection - Mucormycosis in 2% of patients .

Klebsiella species is the predominant bacterial infection identified followed by Pseudomonas infection. Among malignancies, Squamous cell variety is the predominant type followed by Adenocarcinoma and small cell carcinoma.

BAL fluid cytology revealed malignancy in 9%(n=6) of patients. FOB guided Brush cytology revealed malignancy in 10 % (n=7) of patients. TBLB diagnosed etiology of NRP in 68% (n=24 / 35) patients.

In my study, out of 68 patients,41.1% patients were diabetic and 51.47% were found to be smokers. Diabetes is predominantly associated with infectious etiology.No major complications were encountered during FOB in my study.Thus FOB is a useful diagnostic tool in evaluation of patients with non resolving pneumonia.

CONCLUSION

1.Bronchoscopy have a definitive role (Yield 94%) in the diagnosis of Nonresolving pneumonia.

2.Infectious etiology including tuberculosis(60%) is the most common cause of non resolving pneumonia.

3.Transbronchial lung biopsy(68%) may be recommended for all cases of non resolving pneumonia to rule out malignancy .

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ANNEXURES

NAME: AGE: SEX: M/F I.P.NO:

OCCUPATION: D.O.A: D.O.D

C/O: H/O

1.	PRIOR ATT			
	CAT I	CAT II		
2.	DIABETIC			
	OHA			
3.	SMOKER			
	Beedi	Cigar	Duration	
4.	ALLERGY			

5.	COUGH				
6.	SPUTUM				
	Mucoid	Purulent	Blood		
7.	FEVER				
	LOW	High			
8.	DYSPNEA				
9.	CHEST PAIN				
10	LOW	LOA			
11	OTHER . S				

INVESTIGATIONS:

CBC								RFT		LFT	EL.,
TC	DC			PCV	HB	RBC	ESR	PLT	U	C		

1. ICTC : PLEURAL FLUID :
2. SPUTUM AFB :
3. C & S : HBSAG, HCV :

4. FNAC : CT CHEST :
5. BIOPSY :
6. CHEST X-RAY

GIVEN TREATMENT:

1. ANTIBIOTICW
   IV / ORAL
   DURATION
2. OTHER TREATMENT S

FOR Findings:

DATE :

RESULTS :

1. BRONICHIAL WASH / BAL
   - CELLCOUNT :
   - CYTOLOGY :
   - CULTURE SENSITIVITY :
   - GRAM STAIN :
   - AFB SMEAR :
2. BRONCHIAL BRUSH :
3. TBLB :
4. TBNA :
5. POST FOB SPUTUM AFB :
6. POST FOB CHEST X-RAY :

FINAL DIAGNOSIS:

REMARKS:

ஒப்புதல் படிவம்

எனது நுரையீரலில் சளி சேர்ந்து இருப்பதை மருத்துகள் மூலம் அறிந்துகொண்டேன். ஆதன் காரணத்தை கண்டறிய நுரையீரல் உள்நோக்கு கருவியின் (Bronchoscopy) மூலமாக சளி எடுத்து பரிசோதனை செய்ய அறிவுறுத்தப்பட்டது. அப்பரிசோதனை செய்யும் பொழுது. மூச்சு திணறலோ, இரத்த கசிவோ. நுரையீரல் சுற்றி காற்று சேரவோ வாய்ப்பு உள்ளது என்பதை மருத்துவர் விளக்கினார். இருப்பினும் நோயின் தன்மையை அறிய மருத்துவர் மேற்கொள்ளும் இப்பரிசோதனைக்கு முழு மணதுடன் சம்மதிக்கிறேன். இதன்மூலம் ஏற்படும் விளைவுக்கு மருத்துவரோ, மருத்துவ நிர்வாகமோ பொறுப்பாகாது என்பதை ஏற்றுக்கொள்கிறேன்.

நாள் :

இடம்:

இப்படிக்கு

(நோயாளி / உறவினரின் கையொப்பம்)

SL.NO.	NAME	AGE	SEX	CT CHEST	FOB	CYTOLOGY	BAL CULTURE	AFB SMEAR	CBNAAT	BRUSH	TBLB	USG GUIDED FNAC	ETIOLOGY	FINAL DIAGNOSIS	PRIOR ATT	DIABETIC	SMOKER	OTHER COMORBID CONDITIO	HYPER TENSION
1	BALASUBRAMANIYAN	40	M	RT LOWERLOBE	NARROW &IIREGULAR LUMEN	INFLAMMATORY	NEGATIVE	NEGATIVE	NA	POSITIVE	NA	NA	SQUAMOUS CELL CARCINOMA	MALIGNANCY	NO	NO	YES	NO	NO
2	PALANIAMMAL	50	F	LT LOWER LOBE	MASS	INFLAMMATORY	NEGATIVE	NEGATIVE	NA	NEGATIVE	POSITIVE	NA	SQUAMOUS CELL CARCINOMA	MALIGNANCY	NO	NO	NO	NO	NO
3	PITCHAIKANNU	62	M	RT LOWERLOBE	MUCOID	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NEGATIVE	NA	KLEBSIELLA	INFECTIVE	NO	NO	NO	CA ESOPHAGUS	YES
4	THIRUNAVUKARASU	52	M	LT LOWER LOBE	MUCOPURULENT	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NEGATIVE	NA	KLEBSIELLA	INFECTIVE	NO	YES	YES	NO	NO
5	CHELLADURAI	50	M	RT UPPER LOBE	NORMAL	INFLAMMATORY	PSEUDOMANAS	NEGATIVE	NA	NEGATIVE	NA	NA	PSEUDOMONAS AERUGINOSA	INFECTIVE	YES	NO	NO	COPD	NO
6	AMARAVATHY	67	F	RT LOWERLOBE	MUCOPURULENT	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NA	NA	KLEBSIELLA	INFECTIVE	NO	YES	NO	CKD	YES
7	MAHESH	31	M	LT LOWER LOBE	MUCOPURULENT	INFLAMMATORY	PSEUDOMANAS	NEGATIVE	NA	NEGATIVE	NA	NA	PSEUDOMONAS AERUGINOSA	INFECTIVE	NO	NO	YES	NO	NO
8	PANDARAM	75	M	RT MIDDLE LOBE	MUCOPURULENT	INFLAMMATORY	PSEUDOMANAS	NEGATIVE	NA	NEGATIVE	NA	NA	PSEUDOMONAS AERUGINOSA	INFECTIVE	NO	NO	NO	NO	NO
9	AMUDHA	14	F	LT LOWER LOBE	MUCOPURULENT	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NA	NA	KLEBSIELLA	INFECTIVE	NO	YES	NO	NO	NO
10	IMMANUVEL JAMES	62	M	RT LOWERLOBE	NORMAL	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NEGATIVE	NA	KLEBSIELLA	INFECTIVE	NO	NO	YES	COPD	YES
11	GANAPATHY	49	M	RT UPPER LOBE	MUCOPURULENT	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NA	NA	KLEBSIELLA	INFECTIVE	YES	NO	YES	POST RENAL TRANSPLANT	NO
12	PERATCHI	52	M	RT LOWERLOBE	NORMAL	INFLAMMATORY	NEGATIVE	POSITIVE	NA	NEGATIVE	POSITIVE	NA	PTB	INFECTIVE	NO	NO	YES	B/L PLEURAL EFFUSION	NO
13	ALWAR	40	M	RT UPPER LOBE	NORMAL	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NA	NA	KLEBSIELLA	INFECTIVE	YES	YES	YES	CKD	YES
14	MADASAMY	52	M	RT LOWERLOBE	MUCOPURULENT	INFLAMMATORY	PSEUDOMANAS	NEGATIVE	NA	NEGATIVE	NA	NA	PSEUDOMONAS AERUGINOSA	INFECTIVE	YES	YES	NO	NO	YES
15	ANTONYSAMY	72	M	LT UPPER LOBE	MASS	INFLAMMATORY	NEGATIVE	NEGATIVE	NA	NEGATIVE	POSITIVE	NA	SQUAMOUS CELL CARCINOMA	MALIGNANCY	NO	NO	YES	COPD	YES
16	PARAMASIVAN	54	M	RT LOWERLOBE	MASS	INFLAMMATORY	NEGATIVE	NEGATIVE	NA	POSITIVE	NA	NA	SQUAMOUS CELL CARCINOMA	MALIGNANCY	NO	YES	YES	COPD	NO
17	VIKADASUDALAI	70	M	LT UPPER LOBE	NARROW &IIREGULAR LUMEN	MALIGANACY	NEGATIVE	NEGATIVE	NA	NEGATIVE	POSITIVE	NA	SQUAMOUS CELL CARCINOMA	MALIGNANCY	NO	NO	YES	COPD	YES
18	PAULRAJ	67	M	RT LOWERLOBE	MUCOPURULENT	INFLAMMATORY	NEGATIVE	NEGATIVE	NA	NEGATIVE	NEGATIVE	POSITIVE	ADENO CARCINOMA	NO T DIAGNOSED	NO	YES	YES	CAD	YES
19	UDAIYAR	70	M	RT LOWERLOBE	NORMAL	INFLAMMATORY	NEGATIVE	NEGATIVE	NA	NEGATIVE	NEGATIVE	POSITIVE	ADENO CARCINOMA	NO T DIAGNOSED	NO	NO	YES	NO	NO
20	ARUMUGANAINAR	50	M	RT LOWERLOBE	MUCOPURULENT	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NEGATIVE	NA	KLEBSIELLA	INFECTIVE	NO	NO	NO	NO	NO
21	SUDALIMUTHU	61	M	RT UPPER LOBE	MASS	*INFLAMMATORY*	NEGATIVE	POSITIVE	NA	NEGATIVE	POSITIVE	NA	PTB&SQUAMOUS CELL CARCINOMA	COMBINED ETIOLOGY	NO	YES	YES	NO	YES
22	PONROSI	16	F	MULTI LOBAR	MASS	INFLAMMATORY	NEGATIVE	POSITIVE	NA	NEGATIVE	POSITIVE	NA	PTB	INFECTIVE	NO	NO	NO	NO	NO

SL.NO.	NAME	AGE	SEX	CT CHEST	FOB	CYTOLOGY	BAL CULTURE	AFB SMEAR	CBNAAT	BRUSH	TBLB	USG GUIDED FNAC	ETIOLOGY	FINAL DIAGNOSIS	PRIOR ATT	DIABETIC	SMOKER	OTHER COMORBID CONDITIO	HYPER TENSION
23	KRISHNAVENI	48	F	RT LOWERLOBE	NARROW &IIREGULAR LUMEN	INFLAMMATORY	NEGATIVE	POSITIVE	NA	NEGATIVE	POSITIVE	NA	PTB&SQUAMOUS CELL CARCINOMA	COMBINED ETIOLOGY	NO	NO	NO	NO	NO
24	PITCHUMANI	58	M	RT UPPER LOBE	NORMAL	INFLAMMATORY	NEGATIVE	POSITIVE	NA	NEGATIVE	NA	NA	PTB	INFECTIVE	YES	NO	YES	CKD	YES
25	KRISHNAMMAL	62	F	LT UPPER LOBE	NARROW &IIREGULAR LUMEN	INFLAMMATORY	NEGATIVE	POSITIVE	NA	NEGATIVE	NA	NA	PTB	INFECTIVE	NO	YES	NO	CAD	YES
26	PETCHAMMAL	40	F	LT UPPER LOBE	MUCOID	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NA	NA	KLEBSIELLA	INFECTIVE	NO	NO	NO	NO	NO
27	SUYUMBULINGAM	61	M	RT UPPER LOBE	NARROW &IIREGULAR LUMEN	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	POSITIVE	NA	SQUAMOUS CELL CARCINOMA &KLEBSIELLA	COMBINED ETIOLOGY	NO	NO	YES	COPD	NO
28	SHAHUL HAMEED	39	M	RT UPPER LOBE	MASS	INFLAMMATORY	NEGATIVE	NEGATIVE	NA	POSITIVE	NA	NA	SQUAMOUS CELL CARCINOMA	MALIGNANCY	YES	YES	NO	NO	NO
29	SUNDARAJAN	65	M	LINGULAR	MUCOPURULENT	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NA	NA	KLEBSIELLA	INFECTIVE	NO	YES	YES	CAD	YES
30	DESING	54	M	RT UPPER LOBE	MASS	INFLAMMATORY	NEGATIVE	NEGATIVE	NA	POSITIVE	NA	NA	SQUAMOUS CELL CARCINOMA	MALIGNANCY	NO	NO	YES	COPD	NO
31	MANI	55	M	LINGULAR	MUCOPURULENT	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NA	NA	KLEBSIELLA	INFECTIVE	NO	YES	NO	NO	NO
32	MURUGAN	40	M	RT LOWERLOBE	MASS	INFLAMMATORY	NEGATIVE	NEGATIVE	NA	POSITIVE	POSITIVE	NA	SMALL CELL CARCINOMA	MALIGNANCY	NO	NO	YES	NO	NO
33	SHENBEGARAJ	30	M	LT LOWER LOBE	MASS	INFLAMMATORY	NEGATIVE	NEGATIVE	NA	NEGATIVE	POSITIVE	NA	SQUAMOUS CELL CARCINOMA	MALIGNANCY	NO	YES	YES	NO	NO
34	MUTHUESAKKI	45	M	RT MIDDLE LOBE	NORMAL	INFLAMMATORY	CONS	POSITIVE	NA	NEGATIVE	NA	NA	PTB &CONS	COMBINED ETIOLOGY	YES	YES	YES	CKD	YES
35	MURUGAN	37	M	RT MIDDLE LOBE	NORMAL	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NA	NA	KLEBSIELLA	INFECTIVE	NO	NO	YES	NO	NO
36	ANNAMALAI	58	M	RT UPPER LOBE	MUCOPURULENT	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NA	NA	KLEBSIELLA	INFECTIVE	NO	YES	NO	CKD	YES
37	PARAMASIVAN	34	M	LT UPPER LOBE	NORMAL	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NA	NA	KLEBSIELLA	INFECTIVE	NO	NO	NO	NO	NO
38	PETCHAMMAL	68	F	RT LOWERLOBE	NARROW &IIREGULAR LUMEN	INFLAMMATORY	PSEUDOMANAS	NEGATIVE	NA	NEGATIVE	NA	NA	PSEUDOMONAS AERUGINOSA	INFECTIVE	NO	NO	NO	NO	NO
39	ARUMUGAM	65	M	LT LOWER LOBE	MUCOPURULENT	INFLAMMATORY	PSEUDOMANAS	NEGATIVE	NA	NEGATIVE	NA	NA	PSEUDOMONAS AERUGINOSA	INFECTIVE	YES	YES	NO	NO	NO
40	ALAGAMMAL	60	F	RT UPPER LOBE	NARROW &IIREGULAR LUMEN	INFLAMMATORY	NEGATIVE	NEGATIVE	NA	NEGATIVE	POSITIVE	NA	ADENO CARCINOMA	MALIGNANCY	NO	YES	NO	NO	NO
41	SOKKALINGAM	70	M	RT LOWERLOBE	NORMAL	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NA	NA	KLEBSIELLA	INFECTIVE	NO	NO	YES	NO	NO
42	SEENIPANDI	65	M	RT LOWERLOBE	MASS	MALIGANACY	NEGATIVE	NEGATIVE	NA	POSITIVE	POSITIVE	NA	SQUAMOUS CELL CARCINOMA	MALIGNANCY	YES	NO	NO	NO	NO
43	KALIMUTHU	30	M	RT LOWERLOBE	MUCOPURULENT	INFLAMMATORY		NEGATIVE	NA	NEGATIVE	NEGATIVE	NA	KLEBSIELLA	INFECTIVE	NO	YES	NO	NO	NO
44	AVUDAYAPPAN	61	M	RT UPPER LOBE	NARROW &IIREGULAR LUMEN	MALIGANACY	NEGATIVE	NEGATIVE	NA	NEGATIVE	POSITIVE	NA	ADENO CARCINOMA	MALIGNANCY	NO	NO	YES	COPD	NO
45	RAJASEKAR	50	M	RT MIDDLE LOBE	MUCOPURULENT	MALIGANACY	NEGATIVE	NEGATIVE	NA	NEGATIVE	POSITIVE	NA	SQUAMOUS CELL CARCINOMA	MALIGNANCY	NO	NO	YES	COPD	NO
46	KARUNAKARAN	70	M	RT UPPER LOBE	MUCOPURULENT	INFLAMMATORY	PSEUDOMANAS	NEGATIVE	NA	NEGATIVE	NA	NA	PSEUDOMONAS AERUGINOSA	INFECTIVE	YES	YES	YES	COPD	YES

SL.NO.	NAME	AGE	SEX	CT CHEST	FOB	CYTOLOGY	BAL CULTURE	AFB SMEAR	CBNAAT	BRUSH	TBLB	USG GUIDED FNAC	ETIOLOGY	FINAL DIAGNOSIS	PRIOR ATT	DIABETIC	SMOKER	OTHER COMORBID CONDITIO	HYPER TENSION
47	SHENBEGARAJ	48	M	LT LOWER LOBE	NORMAL	INFLAMMATORY	KLEBSIELLA	NEGATIVE	NA	NEGATIVE	NA	NA	KLEBSIELLA	INFECTIVE	NO	YES	NO	NO	NO
48	ERUTHIYARAJ	79	M	RT UPPER LOBE	MUCOID	INFLAMMATORY	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	POSITIVE	NA	MUCORMYCOSIS	INFECTIVE	NO	NO	NO	NO	NO
49	GURUSAMY	70	M	LT LOWER LOBE	MUCOPURULENT	INFLAMMATORY	PSEUDOMANAS	NEGATIVE	NA	NEGATIVE	NA	NA	PSEUDOMONAS AERUGINOSA	INFECTIVE	YES	YES	NO	NO	NO
50	MUTHUKRISHNAN	66	M	MULTI LOBAR	MUCOPURULENT	INFLAMMATORY	NEGATIVE	NEGATIVE	POSITIVE	NEGATIVE	NA	NA	PTB	INFECTIVE	NO	YES	YES	OLD CVA	NO
51	ANTONYSAMY	47	M	RT LOWERLOBE	NORMAL	INFLAMMATORY	NEGATIVE	POSITIVE	NA	NEGATIVE	NA	NA	PTB	INFECTIVE	NO	YES	YES	CKD	YES
52	JEYAPAUL	52	M	RT UPPER LOBE	MUCOPURULENT	INFLAMMATORY	NEGATIVE	POSITIVE	NA	NEGATIVE	NA	NA	PTB	INFECTIVE	NO	YES	YES	RT ISOMERISM	NO
53	CHELLAYA ASARI	75	M	RT LOWERLOBE	MASS	INFLAMMATORY	NEGATIVE	NEGATIVE	NEGATIVE	POSITIVE	POSITIVE	NA	SQUAMOUS CELL CARCINOMA	MALIGNANCY	NO	YES	YES	CORPULMONALE	NO
54	CHELLAPANDI	51	M	LT UPPER LOBE	MASS	MALIGANACY	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	POSITIVE	NA	SQUAMOUS CELL CARCINOMA	MALIGNANCY	NO	YES	YES	CKD	YES
55	PERIYASAMY	53	M	LT LOWER LOBE	NORMAL	MALIGANACY	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	POSITIVE	NA	SQUAMOUS CELL CARCINOMA	MALIGNANCY	NO	NO	NO	NO	NO
56	SHANMUGAVEL	70	M	RT UPPER LOBE	MUCOID	INFLAMMATORY	NEGATIVE	NEGATIVE	NA	NEGATIVE	POSITIVE	NA	PTB	INFECTIVE	NO	NO	YES	CKD	YES
57	PETCHI	60	M	RT LOWERLOBE	NORMAL	INFLAMMATORY	NEGATIVE	NEGATIVE	NA	NEGATIVE	POSITIVE	NA	ADENO CARCINOMA	MALIGNANCY	NO	YES	YES	COPD	YES
58	RAMASAMY	65	M	LT UPPER LOBE	NORMAL	INFLAMMATORY	NEGATIVE	POSITIVE	NA	NEGATIVE	NA	NA	PTB	INFECTIVE	YES	YES	YES	NO	NO
59	JEYAPAUL	47	M	RT UPPER LOBE	MUCOPURULENT	INFLAMMATORY	NEGATIVE	POSITIVE	NA	NEGATIVE	NA	NA	PTB	INFECTIVE	NO	NO	YES	NO	NO
60	KALYANA SUNDARAM	60	M	MULTI LOBAR	NORMAL	INFLAMMATORY	NEGATIVE	NEGATIVE	NA	NEGATIVE	POSITIVE	NA	INTERSTITIAL PNEUMONITIS	INTERSTIAL PNEUMONITIS	YES	NO	YES	CORPULMONALE	NO
61	VEL	40	M	RT LOWERLOBE	MUCOID	INFLAMMATORY	PSEUDOMANAS	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NA	PSEUDOMONAS AERUGINOSA	INFECTIVE	YES	NO	NO	NO	NO
62	VASANTHA	35	F	RT UPPER LOBE	MUCOID	INFLAMMATORY	NEGATIVE	NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE	NA	PTB	INFECTIVE	NO	NO	NO	NO	NO
63	RAMAN	50	M	LT LOWER LOBE	MUCOID	INFLAMMATORY	NEGATIVE	NEGATIVE	NA	NEGATIVE	NEGATIVE	POSITIVE	ADENO CARCINOMA	NO T DIAGNOSED	YES	NO	NO	COPD	YES
64	MUTHIAH	65	M	RT LOWERLOBE	MUCOPURULENT	INFLAMMATORY	NEGATIVE	NEGATIVE	POSITIVE	NEGATIVE	NEGATIVE	NA	PTB	INFECTIVE	NO	NO	NO	NO	NO
65	LEELAVATHY	56	F	RT UPPER LOBE	MASS	INFLAMMATORY	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	POSITIVE	NA	ADENO CARCINOMA	MALIGNANCY	NO	NO	NO	NO	NO
66	SUBBAMAL	52	F	RT LOWERLOBE	MUCOPURULENT	INFLAMMATORY	NEGATIVE	POSITIVE	POSITIVE	NEGATIVE	POSITIVE	NA	PTB	INFECTIVE	NO	NO	NO	BRONCHIECTASIS	NO
67	ESWARI	48	F	LT UPPER LOBE	NORMAL	INFLAMMATORY	NEGATIVE	NEGATIVE	POSITIVE	NEGATIVE	POSITIVE	NA	PTB	INFECTIVE	NO	NO	NO	NO	NO
68	KALAVATHY	55	F	RT LOWERLOBE	MUCOID	INFLAMMATORY	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NEGATIVE	NA	NO DIAGNOSIS	NO T DIAGNOSED	NO	NO	NO	NO	NO